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(54) Title: DIAMINE DERIVATIVES OF QUINONE AND USES THEREOF

(57) Abstract: Diamine derivatives of quinones, and related compounds, including salts thereof, that modulate the levels of gene expression in cellular systems, such as cancer cells, are disclosed, along with methods for preparing such compounds and derivatives, as well as pharmaceutical compositions containing these compounds and derivatives as active ingredients. Methods of using these as compounds and derivatives as therapeutic agents are also described.

WO 2005/016264 A2

Diamine Derivatives of Quinone and Uses Thereof

This application claims priority of U.S. Provisional Application Serial No. 60/492,521, filed 5 August 2003, and 60/523,477, filed 19 November 2003, and U.S. Application Serial No. 10/758,521, filed 15 January 2004, the disclosures of which are hereby incorporated by reference in their entirety.

FIELD OF THE INVENTION

The present invention relates to chemical agents affecting levels of gene expression in cellular systems, including cancer cells. In particular, the present invention relates to derivatives of quinone moiety, processes for their preparation, their use as antitumor drugs and pharmaceutical compositions containing them as active ingredients.

BACKGROUND OF THE INVENTION

Screening assays for novel drugs are based on the response of model cell based systems *in vitro* to treatment with specific compounds. Various measures of cellular response have been utilized, including the release of cytokines, alterations in cell surface markers, activation of specific enzymes, as well as alterations in ion flux and/or pH. Some such screens rely on specific genes, such as oncogenes or tumor suppressors.

Our approach to screening small molecule compounds as potential anticancer drugs is based on the idea that for each specific tumor type, a unique signature set of genes, that are differentially expressed in tumor cells if compared to corresponding normal cells, can be established. The relatively small signature set, containing 10-30 genes, allows for easy, high throughput screening for compounds that can reverse the gene expression profile from patterns typical for cancer cells to patterns seen in normal cells. As a part of our efforts to provide new diversified compounds for high throughput gene expression screening, we designed and synthesized a number of novel derivatives of quinones. Gene expression screening and subsequent cytotoxicity screening revealed that some of the compounds possess biological activity. Consequent, more detailed structure-activity relationship studies led to the discovery of compounds of formula I as new small molecule agents having antineoplastic activity.

BRIEF SUMMARY OF THE INVENTION

In one aspect, the present invention relates to novel organic compounds, derivatives of quinone, that have the ability to function as gene expression modulators for genes found in cancer cells, especially genes involved in misregulated signal transduction pathways typical for cancer such as colon and breast cancers.

In one embodiment of the present invention, the compounds disclosed herein are able to up regulate genes found to be up regulated in normal (i.e., non-cancerous) cells versus cancer cells, especially colon and breast cancer cells, thereby producing an expression profile for said gene(s) that more resembles the expression profile found in normal cells. In another embodiment, the compounds disclosed herein are found to down regulate genes found to be up regulated in cancer cells, especially colon and breast cancer cells, relative to normal (i.e., non-cancerous) cells thereby producing

an expression profile for said gene(s) that more resembles the expression profile found in normal cells. Thus, in addition to activity in modulating a particular gene that may or may not have a major role in inducing or sustaining a cancerous condition, the agents disclosed herein also find value in regulating a set of gene whose combined activity is related to a disease condition, such as cancer, especially colon and breast cancer, including adenocarcinoma of the colon. Thus, while an overall set of genes is modulated, the effect of modulating any subset of these may be disproportionately large or small with respect to the effect in ameliorating the overall disease process. Consequently, different disease conditions may rely on different subsets of genes to be active or inactive as a basis for the overall disease process.

Thus, the present invention relates to novel organic compounds that have the ability to function as gene modulators for genes found in normal (i.e., non-cancer) cells and which genes are found to be up regulated or down regulated in normal cells, especially colon and breast cells. Such an effect may prevent a disease condition, such as cancer, from arising in those otherwise more susceptible to such a condition. In one such embodiment, administration of one or more of the agents disclosed herein may succeed in preventing a cancerous condition from arising.

In other embodiments, the agents disclosed herein find use in combination with each other as well as with other agents, such as where a mixture of one or more of the agents of the present invention are given in combination or where one or more of the agents disclosed herein is given together with some other already known therapeutic agent, possibly as a means of potentiating the affects of such known therapeutic agent or vice versa.

The present invention also relates to processes of preventing or treating disease conditions, especially cancer, most especially colon and

breast cancer, by administering to a subject, such as a mammal, especially a human, a therapeutically active amount of one or more of the agents disclosed herein, including where such agents are given in combination with one or more known therapeutic agents.

DEFINITIONS

The following is a list of definitions for terms used herein.

"Acyl" or "carbonyl" is a radical formed by removal of the hydroxy from a carboxylic acid (i.e., R-C(=O)-). Preferred acyl groups include (for example) acetyl, formyl, and propionyl.

"Alkyl" is a saturated hydrocarbon chain having 1 to 15 carbon atoms, preferably 1 to 10, more preferably 1 to 4 carbon atoms. "Alkene" is a hydrocarbon chain having at least one (preferably only one) carbon-carbon double bond and having 2 to 15 carbon atoms, preferably 2 to 10, more preferably 2 to 4 carbon atoms. "Alkyne" is a hydrocarbon chain having at least one (preferably only one) carbon-carbon triple bond and having 2 to 15 carbon atoms, preferably 2 to 10, more preferably 2 to 4 carbon atoms. Alkyl, alkene and alkyne chains (referred to collectively as "hydrocarbon chains") may be straight or branched and may be unsubstituted or substituted. Preferred branched alkyl, alkene and alkyne chains have one or two branches, preferably one branch. Preferred chains are alkyl. Alkyl, alkene and alkyne hydrocarbon chains each may be unsubstituted or substituted with from 1 to 4 substituents; when substituted, preferred chains are mono-, di-, or tri-substituted. Alkyl, alkene and alkyne hydrocarbon chains each may be substituted with halo, hydroxy, aryloxy (*e.g.,* phenoxy), heteroaryloxy, acyloxy (e.g., acetoxy), carboxy, aryl (*e.g.,* phenyl), heteroaryl, cycloalkyl, heterocycloalkyl, spirocycle, amino, amido, acylamino, keto, thioketo, cyano,

or any combination thereof. Preferred hydrocarbon groups include methyl, ethyl, propyl, isopropyl, butyl, vinyl, allyl, butenyl, and exomethylenyl.

Also, as referred to herein, a "lower" alkyl, alkene or alkyne moiety (e.g., "lower alkyl") is a chain comprised of 1 to 6, preferably from 1 to 4, carbon atoms in the case of alkyl and 2 to 6, preferably 2 to 4, carbon atoms in the case of alkene and alkyne.

"Alkoxy" is an oxygen radical having a hydrocarbon chain substituent, where the hydrocarbon chain is an alkyl or alkenyl (i.e., -O-alkyl or -O-alkenyl). Preferred alkoxy groups include (for example) methoxy, ethoxy, propoxy and allyloxy.

"Aryl" is an aromatic hydrocarbon ring. Aryl rings are monocyclic or fused bicyclic ring systems. Monocyclic aryl rings contain 6 carbon atoms in the ring. Monocyclic aryl rings are also referred to as phenyl rings. Bicyclic aryl rings contain from 8 to 17 carbon atoms, preferably 9 to 12 carbon atoms, in the ring. Bicyclic aryl rings include ring systems wherein one ring is aryl and the other ring is aryl, cycloalkyl, or heterocycloakyl. Preferred bicyclic aryl rings comprise 5-, 6- or 7-membered rings fused to 5-, 6-, or 7-membered rings. Aryl rings may be unsubstituted or substituted with from 1 to 4 substituents on the ring. Aryl may be substituted with halo, cyano, nitro, hydroxy, carboxy, amino, acylamino, alkyl, heteroalkyl, haloalkyl, phenyl, aryloxy, alkoxy, heteroalkyloxy, carbamyl, haloalkyl, methylenedioxy, heteroaryloxy, or any combination thereof. Preferred aryl rings include naphthyl, tolyl, xylyl, and phenyl. The most preferred aryl ring radical is phenyl.

"Aryloxy" is an oxygen radical having an aryl substituent (i.e., -O-aryl). Preferred aryloxy groups include (for example) phenoxy, napthyloxy, methoxyphenoxy, and methylenedioxyphenoxy.

"Cycloalkyl" is a saturated or unsaturated hydrocarbon ring. Cycloalkyl rings are not aromatic. Cycloalkyl rings are monocyclic, or are fused, spiro, or bridged bicyclic ring systems. Monocyclic cycloalkyl rings contain from about 3 to about 9 carbon atoms, preferably from 3 to 7 carbon atoms, in the ring. Bicyclic cycloalkyl rings contain from 7 to 17 carbon atoms, preferably from 7 to 12 carbon atoms, in the ring. Preferred bicyclic cycloalkyl rings comprise 4-, 5- 6- or 7-membered rings fused to 5-, 6-, or 7-membered rings. Cycloalkyl rings may be unsubstituted or substituted with from 1 to 4 substituents on the ring. Cycloalkyl may be substituted with halo, cyano, alkyl, heteroalkyl, haloalkyl, phenyl, keto, hydroxy, carboxy, amino, acylamino, aryloxy, heteroaryloxy, or any combination thereof. Preferred cycloalkyl rings include cyclopropyl, cyclopentyl, and cyclohexyl.

"Halo" or "halogen" is fluoro, chloro, bromo or iodo. Preferred halo are fluoro, chloro and bromo; more preferred typically are chloro and fluoro, especially fluoro.

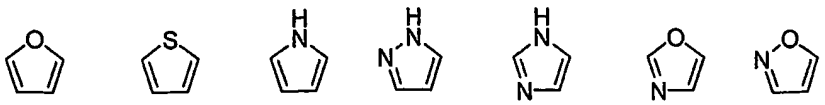
"Haloalkyl" is a straight, branched, or cyclic hydrocarbon substituted with one or more halo substituents. Preferred are C_1-C_{12} haloalkyls; more preferred are C_1-C_6 haloalkyls; still more preferred still are C_1-C_3 haloalkyls. Preferred halo substituents are fluoro and chloro. The most preferred haloalkyl is trifluoromethyl.

"Heteroatom" is a nitrogen, sulfur, or oxygen atom. Groups containing more than one heteroatom may contain different heteroatoms.

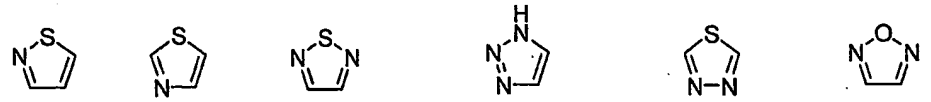
"Heteroalkyl" is a saturated or unsaturated chain containing carbon and at least one heteroatom, wherein no two heteroatoms are adjacent. Heteroalkyl chains contain from 2 to 15 member atoms (carbon and heteroatoms) in the chain, preferably 2 to 10, more preferably 2 to 5. For example, alkoxy (i.e., -O-alkyl or -O-heteroalkyl) radicals are included in heteroalkyl. Heteroalkyl chains may be straight or branched. Preferred

branched heteroalkyl have one or two branches, preferably one branch. Preferred heteroalkyl are saturated. Unsaturated heteroalkyl have one or more carbon-carbon double bonds and/or one or more carbon-carbon triple bonds. Preferred unsaturated heteroalkyls have one or two double bonds or one triple bond, more preferably one double bond. Heteroalkyl chains may be unsubstituted or substituted with from 1 to 4 substituents. Preferred substituted heteroalkyl are mono-, di-, or tri-substituted. Heteroalkyl may be substituted with lower alkyl, haloalkyl, halo, hydroxy, aryloxy, heteroaryloxy, acyloxy, carboxy, monocyclic aryl, heteroaryl, cycloalkyl, heterocycloalkyl, spirocycle, amino, acylamino, amido, keto, thioketo, cyano, or any combination thereof. Where a group is described, for example, as an alkyl derivative, such as "-ethylpyridine" the dash "-" indicate point of attachment of the substituent. Thus, "-ethylpyridine" means attachment of ethylpyridine via the ethyl portion of the group whereas "ethylpyridine-" means attachment via the pyridinyl ring.

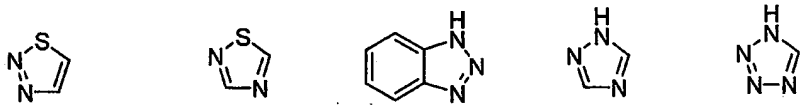
"Heteroaryl" is an aromatic ring containing carbon atoms and from 1 to about 6 heteroatoms in the ring. Heteroaryl rings are monocyclic or fused bicyclic ring systems. Monocyclic heteroaryl rings contain from about 5 to about 9 member atoms (carbon and heteroatoms), preferably 5 or 6 member atoms, in the ring. Bicyclic heteroaryl rings contain from 8 to 17 member atoms, preferably 8 to 12 member atoms, in the ring. Bicyclic heteroaryl rings include ring systems wherein one ring is heteroaryl and the other ring is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl. Preferred bicyclic heteroaryl ring systems comprise 5-, 6- or 7-membered rings fused to 5-, 6-, or 7-membered rings. Heteroaryl rings may be unsubstituted or substituted with from 1 to 4 substituents on the ring. Heteroaryl may be substituted with halo, cyano, nitro, hydroxy, carboxy, amino, acylamino, alkyl, heteroalkyl, haloalkyl, phenyl, alkoxy, aryloxy, heteroaryloxy, or any combination thereof. Preferred heteroaryl rings include, but are not limited to, the following:



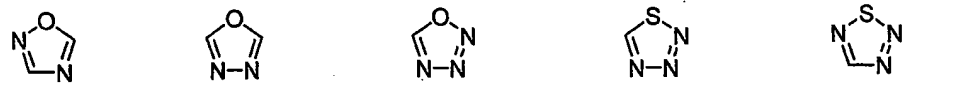
Furan Thiophene Pyrrole Pyrazole Imidazole Oxazole Isoxazole



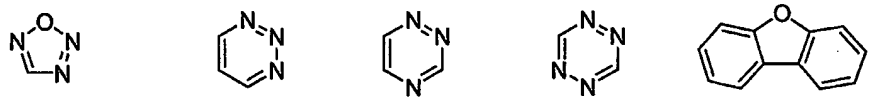
Isothiazole Thiazole 1,2,5-Thiadiazole 1,2,3-Triazole 1,3,4-Thiadiazole Furazan



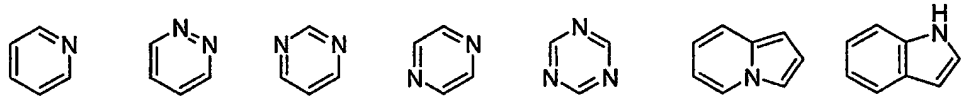
1,2,3-Thiadiazole 1,2,4-Thiadiazole Benzotriazole 1,2,4-Triazole Tetrazole



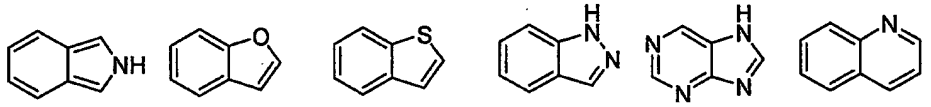
1,2,4-Oxadiazole 1,3,4-Oxadiazole 1,2,3,4-Oxatriazole 1,2,3,4-Thiatriazole 1,2,3,5-Thiatriazole



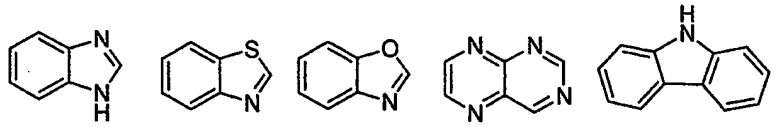
1,2,3,5-Oxatriazole 1,2,3-Triazine 1,2,4-Triazine 1,2,4,5-Tetrazine Dibenzofuran



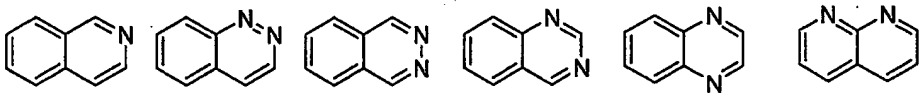
Pyridine Pyridazine Pyrimidine Pyrazine 1,3,5-Triazine Indolizine Indole



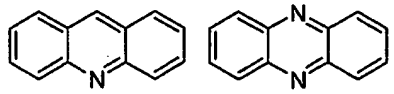
Isoindole Benzofuran Benzothiophene 1H-Indazole Purine Quinoline



Benzimidazole Benzthiazole Benzoxazole Pteridine Carbazole



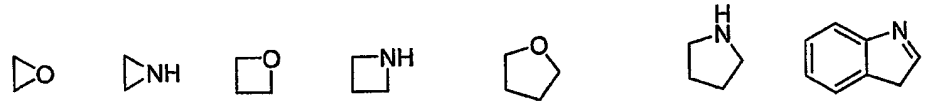
Isoquinoline Cinnoline Phthalazine Quinazoline Quinoxaline 1,8-Napthypyridine



Acridine Phenazine

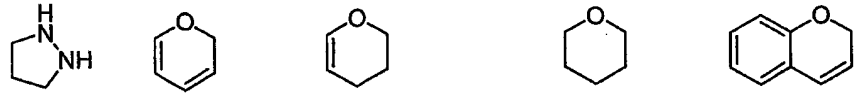
"Heteroaryloxy" is an oxygen radical having a heteroaryl substituent (i.e., -O-heteroaryl). Preferred heteroaryloxy groups include (for example) pyridyloxy, furanyloxy, (thiophene)oxy, (oxazole)oxy, (thiazole)oxy, (isoxazole)oxy, pyrmidinyloxy, pyrazinyloxy, and benzothiazolyloxy.

"Heterocycloalkyl" is a saturated or unsaturated ring containing carbon atoms and from 1 to about 4 (preferably 1 to 3) heteroatoms in the ring. Heterocycloalkyl rings are not aromatic. Heterocycloalkyl rings are monocyclic, or are fused, bridged, or spiro bicyclic ring systems. Monocyclic heterocycloalkyl rings contain from about 3 to about 9 member atoms (carbon and heteroatoms), preferably from 5 to 7 member atoms, in the ring. Bicyclic heterocycloalkyl rings contain from 7 to 17 member atoms, preferably 7 to 12 member atoms, in the ring. Bicyclic heterocycloalkyl rings contain from about 7 to about 17 ring atoms, preferably from 7 to 12 ring atoms. Bicyclic heterocycloalkyl rings may be fused, spiro, or bridged ring systems. Preferred bicyclic heterocycloalkyl rings comprise 5-, 6- or 7-membered rings fused to 5-, 6-, or 7-membered rings. Heterocycloalkyl rings may be unsubstituted or substituted with from 1 to 4 substituents on the ring. Heterocycloalkyl may be substituted with halo, cyano, hydroxy, carboxy, keto, thioketo, amino, acylamino, acyl, amido, alkyl, heteroalkyl, haloalkyl, phenyl, alkoxy, aryloxy or any combination thereof. Preferred substituents on heterocycloalkyl include halo and haloalkyl. Preferred heterocycloalkyl rings include, but are not limited to, the following:

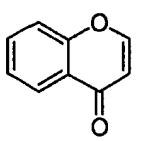


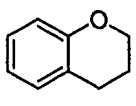
Oxirane Aziridine Oxetane Azetidine Tetrahydrofuran Pyrrolidine 3H-Indole

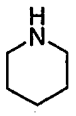
1,3-Dioxolane 1,2-Dithiolane 1,3-Dithiolane 4,5-Dihydroisoxazole 2,3-Dihydroisoxazole

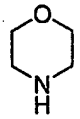


Pyrazolidine 2*H*-Pyran 3,4-Dihydro-2*H*-pyran Tetrahydropyran 2*H*-Chromene


Chromone


Chroman

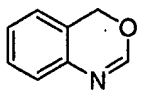

Piperidine

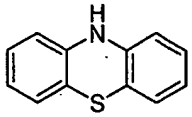

Morpholine


4*H*-1,3-Oxazine

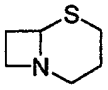

6*H*-1,3-Oxazine

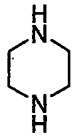

5,6-dihydro-4*H*-1,3-oxazine


4*H*-3,1-benzoxazine


Phenothiazine


1,3-Dioxane


Cepham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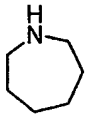
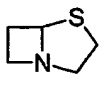
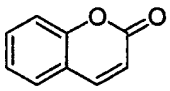
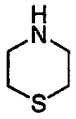

Hexahydroazepine

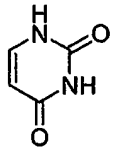

1,3-Dithiane


1,4-Dioxane


Penem


Coumarin


Thiomorpholine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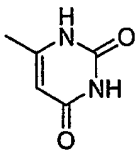
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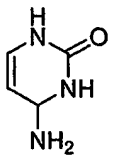
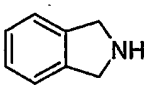
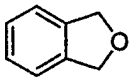

Cytosine

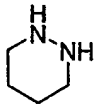

Thiolane

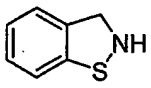

2,3-Dihydro-1*H*-Isoindole

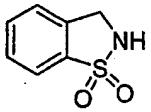

Phthalan


1,4-Oxathiane


1,4-Dithiane


hexahydro-Pyridazine


1,2-Benzisothiazoline


Benzylsultam

While alkyl, heteroalkyl, cycloalkyl, and heterocycloalkyl groups may be substituted with hydroxy, amino, and amido groups as stated above, the following are not envisioned in the invention:

Enols (OH attached to a carbon bearing a double bond).

Amino groups attached to a carbon bearing a double bond (except for vinylogous amides).

More than one hydroxy, amino, or amido attached to a single carbon (except where two nitrogen atoms are attached to a single carbon atom and all three atoms are member atoms within a heterocycloalkyl ring).

Hydroxy, amino, or amido attached to a carbon that also has a heteroatom attached to it.

A "pharmaceutically-acceptable salt" is a cationic salt formed at any acidic (e.g., carboxylic acid) group, or an anionic salt formed at any basic (e.g., amino) group. Many such salts are known in the art, as described in World Patent Publication 87/05297, Johnston et al., published September 11, 1987 incorporated by reference herein. Preferred cationic salts include the alkali metal salts (such as sodium and potassium), and alkaline earth metal salts (such as magnesium and calcium) and organic salts. Preferred anionic salts include the halides (such as chloride salts), sulfonates, carboxylates, phosphates, and the like.

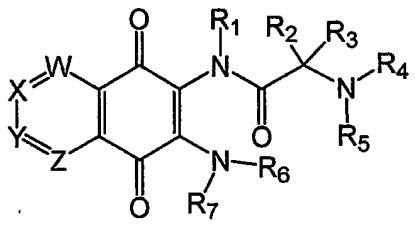
Such salts are well understood by the skilled artisan, and the skilled artisan is able to prepare any number of salts given the knowledge in the art. Furthermore, it is recognized that the skilled artisan may prefer one salt over another for reasons of solubility, stability, formulation ease and the like. Determination and optimization of such salts is within the purview of the skilled artisan's practice.

A "solvate" is a complex formed by the combination of a solute (e.g., a metalloprotease inhibitor) and a solvent (e.g., water). See J. Honig et al., The Van Nostrand Chemist's Dictionary, p. 650 (1953). Pharmaceutically-acceptable solvents used according to this invention include those that do not interfere with the biological activity of the metalloprotease inhibitor (e.g., water, ethanol, acetic acid, N,N-dimethylformamide and others known or readily determined by the skilled artisan).

The terms "optical isomer", "stereoisomer", and "diastereomer" have the accepted meanings (see, e.g., Hawley's Condensed Chemical Dictionary, 11th Ed.). The illustration of specific protected forms and other derivatives of the compounds of the instant invention is not intended to be limiting. The application of other useful protecting groups, salt forms, etc. is within the ability of the skilled artisan.

DETAILED SUMMARY OF THE INVENTION

The present invention relates generally to a compound having the structure:



Formula I

wherein

W, X, Y and Z are each selected from a bond, CH, C-R_8, C-R_9, C-R_{10}, C-R_{11}, O (oxygen), N (nitrogen) and S (sulfur) and no more than two of W, X, Y and Z are simultaneously O, N and S;

and wherein, R_8, R_9, R_{10}, R_{11} each may be hydrogen, hydroxyl, sulfhydryl, alkoxy, thioalkoxy, alkyl, halogen, CN, CF_3, NO_2, $COOR_{12}$, $CONR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{12}COR_{13}$, $NR_{12}SO_2R_{13}$, and $NR_{14}CONR_{12}R_{13}$;

wherein R_{12}, R_{13} and R_{14} are hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, or heterocycloalkyl;

$NR_{12}R_{13}$ may form a substituted or unsubstituted, mono or bicyclic rings, with one to four heteroatoms selected from N, O and S;

and wherein, R_{12} and R_{14} may form a 4, 5, 6 or 7-membered cyclic ring system;

and wherein R_1, R_2, R_3, R_4, and R_5 are each selected from:

hydrogen, alkyl,

substituted or unsubstituted phenyl or polyaromatic rings,

substituted or unsubstituted heteroaromatic, with hetero atom(s) as N, O, S,

substituted or unsubstituted aralkyl,

substituted or unsubstituted cyclo or polycyclo hydrocarbon and mono or polyheterocycle (3-8 atoms per ring) with one to four hetero atoms as N, O, or S; and

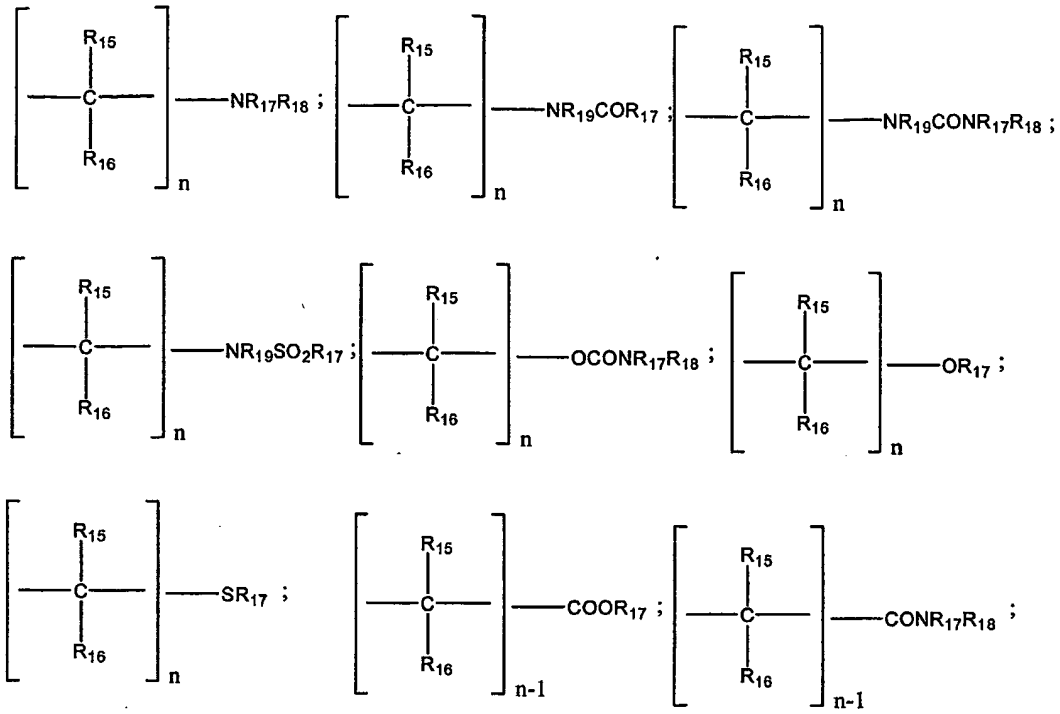
wherein said substitutions are selected from hydroxyl, sulfhydryl, alkoxy, thioalkoxy, alkyl, halogen, CN, CF_3, NO_2, $COOR_{12}$, $CONR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{12}COR_{13}$, $NR_{12}SO_2R_{13}$, and $NR_{14}CONR_{12}R_{13}$;

wherein R_{12}, R_{13} and R_{14} are each selected from hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, and heterocycloalkyl;

$NR_{12}R_{13}$ is also substituted or unsubstituted, mono or bicyclic rings with one to four heteroatoms selected from N, O and S;

and wherein R_{12} and R_{14} may, in one embodiment, form a 4, 5, 6 or 7-membered cyclic ring system;

and wherein R_1, R_4, R_5, R_6 and R_7 may also be selected from:



wherein n is 2, 3 or 4 and R_{15}, R_{16}, R_{17}, R_{18} and R_{19} are selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl, and unsubstituted or substituted alkylaryl;

and $NR_{17}R_{18}$ may also be a substituted or unsubstituted, mono or bicyclic ring with one to four heteroatoms selected from N, O and S;

and wherein R_{17} and R_{19} may form a 4, 5, 6 or 7-membered cyclic ring system;

and wherein R_4 is also selected from $-COR_{13}$, $-SO_2R_{13}$, $-CONR_{12}R_{13}$, and $-C(=NR_{19})NR_{17}R_{18}$;

wherein R_6 and R_7 may also each be selected from:

alkyl,

substituted and unsubstituted phenyl or polyaromatic,

substituted and unsubstituted heteroaromatic rings with hetero atoms selected from N, O and S,
substituted and unsubstituted aralkyl,
substituted and unsubstituted, cyclic or polycyclic hydrocarbon and mono or polyheterocyclic rings, each of 3-8 atoms, said heterocycle having one to four hetero atoms selected from N, O and S; and
wherein substitutions are selected from hydroxyl, sulfhydryl, alkoxy, thioalkoxy, alkyl, halogen, CN, CF_3, NO_2, $COOR_{12}$, $CONR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{12}COR_{13}$, $NR_{12}SO_2R_{13}$, $NR_{14}CONR_{12}R_{13}$;
wherein R_{12}, R_{13} and R_{14} are each selected from hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, and heterocycloalkyl;
$NR_{12}R_{13}$ is also unsubstituted, monosubstituted or polysubstituted mono or bicyclic ring with one to four heteroatoms such as N, O, S;

and wherein NR_4R_5 and NR_6R_7 may each form a substituted or unsubstituted, mono or bicyclic ring comprising one to four heteroatoms selected from N, O and S and wherein said N may also be substituted or unsubstituted,

and including salts of any of the above-recited structures.

In another preferred embodiment, R_1, R_2, R_3, R_4, and R_5 are each selected from hydrogen, alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted polyaromatic, and substituted or unsubstituted heteroaromatic comprising one or more hetero atom(s) selected from N, O and S.

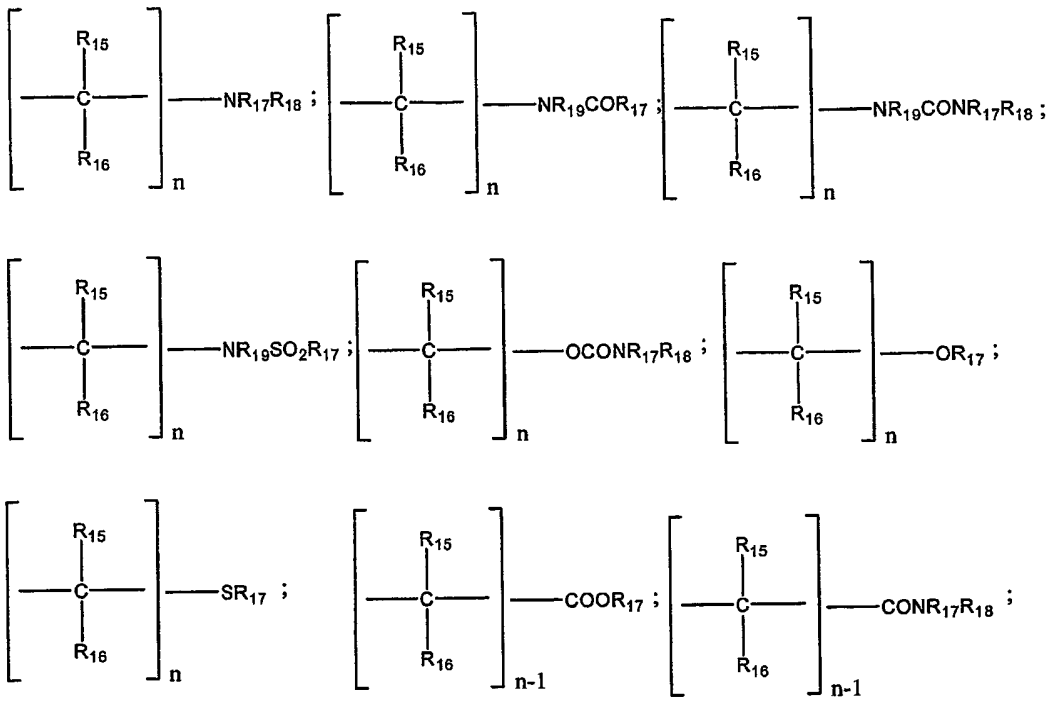
In another preferred embodiment, R_1, R_2, R_3, R_4, and R_5 are each selected from substituted or unsubstituted aralkyl, substituted or unsubstituted

cyclo or polycyclo hydrocarbon or mono or polyheterocycle (3-8 atoms per ring) with one to four hetero atoms selected from N, O and S.

In any of these preferred embodiments, substitutions are selected from hydroxyl, sulfhydryl, lower alkoxy (1-6 carbon), lower thioalkoxy (1-6 carbon), lower alkyl (1-6 carbon), halogen, CN, CF_3, NO_2, $COOR_{12}$, $CONR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{12}COR_{13}$, $NR_{12}SO_2R_{13}$, and $NR_{14}CONR_{12}R_{13}$, wherein R_{12}, R_{13} and R_{14} are hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, or heterocycloalkyl. In a further preferred embodiment of the foregoing, R_{12} and R_{14} form a 4, 5, 6 or 7-member cyclic ring system.

In a further preferred embodiment, $NR_{12}R_{13}$ forms a substituted or unsubstituted mono or bicyclic ring comprising one to four heteroatoms selected from N, O and S.

In one preferred embodiment, R_1, R_4, R_5, R_6 and R_7 are each selected from:



wherein n is 2, 3 or 4 and R_{15}, R_{16}, R_{17}, R_{18} and R_{19} are selected from hydrogen, lower alkyl, cycloalkyl, substituted and unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted alkylaryl. In a preferred embodiment thereof, $NR_{17}R_{18}$ is forms a substituted or unsubstituted, mono or bicyclic ring comprising one to four heteroatoms selected from N, O and S. In another preferred embodiment thereof, R_{17} and R_{19} form a 4, 5, 6 or 7-membered cyclic ring system.

In a preferred embodiment of the compounds of Formula I, W and Z are each selected from C-R_8, C-R_{11} and N, and X and Y are each selected from C-R_9 and C-R_{10}. In another preferred embodiment, X and Y are each selected from C-R_9, C-R_{10} and N and wherein W and Z are each selected from C-R_8 and C-R_{11}. In another preferred embodiment, W is C-R_8 or N, and X, Y and Z are each selected from C-R_9, C-R_{10} and C-R_{11}.

Where a position in a structure, such as W, X, Y or Z, or a substituent, such as an R group, as recited above, is described as selected from, it means

that each of W, X, Y and Z, or R, can be selected from the indicated group of structures or atoms and each is selected independently of the others unless it is expressly stated herein to be otherwise. By "independent" is meant that the selection of one substituent does not limit the range of selection for another substituent, unless expressly stated as such. For example, where X and Y are selected from a range of atoms, such as N, O and S, then X and Y may be the same or different and the selection of one does not limit the range of the other. Thus, if X is nitrogen then Y can still be N, O or S.

Where a position, for example, in a ring, is described as being selected from "a bond" etc., this means that the position is not occupied by an atom. Thus, if in Formula I, X is a bond, then the ring with W, X, Y and Z is a 5 membered ring instead of a 6 membered ring.

In a preferred embodiment, NR_4R_5 and/or NR_6R_7 of Formula I form(s) a piperazine ring, preferably an N-acetylpiperazinyl group.

In a preferred embodiment, $-NR_4R_5$ and/or $-NR_6R_7$ of Formula I is a substituted or unsubstituted morpholinyl group. In a highly preferred embodiment thereof, R_6 and R_7 are both hydrogen. In a most preferred embodiment, R_2 and R_3 are both hydrogen and $-NR_4R_5$ forms an unsubstituted morpholinyl group.

In a preferred embodiment, NR_4R_5 and/or NR_6R_7 of Formula I is a piperidine ring, preferably a substituted piperidine ring, most preferably 4-hydroxypiperidine.

In a highly preferred embodiment of any of the structures of the present invention, R_1, R_6 and R_7 of Formula I are each methyl.

In another preferred embodiment of the compounds of the invention, Z is C-R_{11} or N and W, Y and Z are each selected from C-R_8, C-R_9 and C-R_{10}. In one embodiment of the latter, X is C-R_9 or N and W, Y and Z are each

selected from C-R_8, C-R_{10} and C-R_{11}. In a preferred embodiment of the latter Y is C-R_{10} or N and W, X, and Z are each selected from CH, C-R_8, C-R_9 and C-R_{11}. In a most preferred embodiment thereof, W, X, Y and Z are each selected from CH, C-R_8, C-R_9, C-R_{10} and C-R_{11}, most preferably where W X, Y and Z are each CH (thereby forming a phenyl ring).

In another preferred embodiment of the compounds of the invention, R_2 and R_3 are selected from hydrogen, lower alkyl (1-6 carbon) or aryl. In a further preferred embodiment of the compounds of the invention, R_1 is selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and -alkylpyrrolidine and wherein R_2 and R_3 are selected from hydrogen, lower alkyl (1-6 carbons) and aryl.

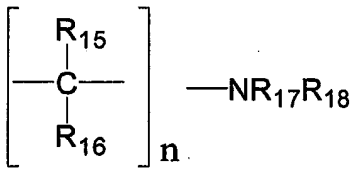
In another preferred embodiment of the compounds of the invention, R_4 and R_5 are each selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl-, N,N-dialkyl-propyl-, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and –alkylpyrrolidine, and wherein R_2 and R_3 are selected from hydrogen, lower alkyl (1-6 carbon) and aryl.

In another preferred embodiment of the compounds of the invention, R_6 and R_7 are selected from alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -

alkylmorpholine, -alkylpiperizine, -alkypiperidine, and –alkylpyrrolidine, and R_2 and R_3 are each selected from hydrogen, lower alkyl (1-6 carbons) and aryl.

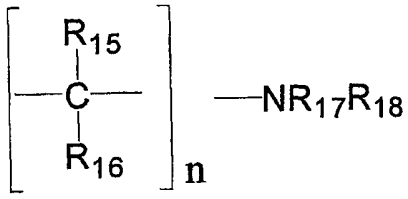
In other preferred embodiments, R_2 and R_3 are selected from hydrogen, lower alkyl (1-6 carbon) and aryl, wherein R_1, R_4 and R_5 are each selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl-, N,N-dialkyl-propyl-, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and –alkylpyrrolidine, and wherein R_2 and R_3 are selected from hydrogen, lower alkyl (1-6 carbon) or aryl and wherein R_6 and R_7 are selected from alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and -alkylpyrrolidine.

In another preferred embodiment of the compounds of the invention having Formula 1, R_2 and R_3 are each selected from hydrogen and alkyl, and wherein R_4 and R_6 are each selected from alkyl and



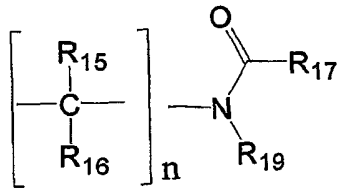
wherein n is 2 ,3 or 4 and wherein one or both of R_5 and R_7 is alkyl, preferably both, and in either case most preferably wherein the alkyl is methyl.

In another preferred embodiment of Formula I, R_1 is alkyl while R_2 and R_3 are each selected from hydrogen and alkyl, and R_4 and R_6 are each selected from alkyl and



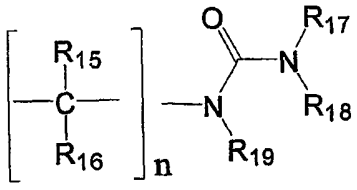
wherein n is 2, 3 or 4 and one or both of R_5 and R_7 is alkyl, preferably both, and in either case most preferably wherein the alkyl is methyl.

In another preferred embodiment of Formula 1, R_2 and R_3 are each selected from hydrogen and alkyl while R_4 and R_6 are each selected from alkyl and



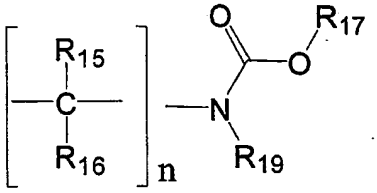
where n is 2, 3 or 4 and one or both of R5 and R7 is alkyl, preferably both, and in either case most preferably wherein the alkyl is methyl.

In another preferred embodiment of Formula 1, R_2 and R_3 are each selected from hydrogen and alkyl, wherein R_4 and R_6 are each selected from alkyl and



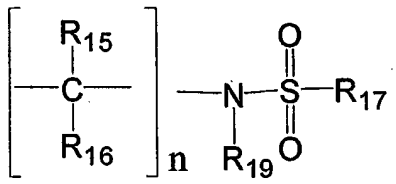
where n is 2, 3 or 4 and at least one of R_5 and R_7 is alkyl, preferably both, and in either case most preferably wherein the alkyl is methyl.

In another preferred embodiment of Formula 1, R_2 and R_3 are each selected from hydrogen and alkyl, and R_4 and R_6 are each selected from alkyl and



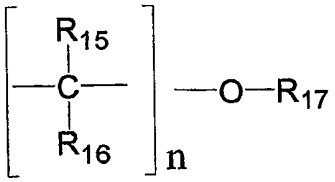
where n is 2, 3 or 4 and at least one of R5 and R7 is alkyl, preferably both, and in either case most preferably wherein the alkyl is methyl.

In another preferred embodiment of Formula 1, R2 and R3 are each selected from hydrogen and alkyl, and R4 and R6 are each selected from alkyl and



wherein n is 2, 3 or 4 and wherein one or both of R_5 and R_7 is alkyl, preferably both, and in either case most preferably wherein the alkyl is methyl.

In another preferred embodiment of Formula 1, R_2 and R_3 are each be hydrogen or alkyl, R_4 and R_6 are each selected from alkyl and



where n is 2, 3 or 4 and one or both of R_5 and R_7 is alkyl, and in either case most preferably wherein the alkyl is methyl.

In separate embodiments, the present invention encompasses compounds having a structure found in Table 1 including salts thereof, a compound having a structure of Table 2 including salts thereof, a compound having a structure of Table 3 including salts thereof, a compound having a structure of Table 4 including salts thereof, a compound having a structure of Table 5 including salts thereof, a compound having a structure of Table 6 including salts thereof, a compound having a structure of Table 7 including salts thereof, a compound having a structure of Table 8 including salts thereof, a compound having a structure of Table 9 including salts thereof, a compound having a structure of Table 11 including salts thereof, a compound having a structure of Table 12 including salts thereof, a compound having a structure of Table 13 including salts thereof, a compound having a structure of Table 14 including salts thereof, a compound having a structure of Table 15 including salts thereof, a compound having a structure of Table 16 including salts thereof, a compound having a structure of Table 17 including salts thereof, and a compound having a structure of Table 18 including salts thereof, and in each case most preferably pharmaceutically acceptable salts thereof. It is to be understood that each of the structures defined in each of these tables is considered to be a separate and preferred embodiment of the present invention.

In another aspect, the present invention relates to compositions of any of the compounds of the invention, preferably wherein such compound is

present in a pharmaceutically acceptable carrier and in a therapeutically effective amount. Such compositions will generally comprise an amount of such compound that is not toxic (i.e., an amount that is safe for therapeutic uses).

In accordance with the foregoing, the present invention is directed to use of the compounds of the invention as active ingredients for medicaments, in particular for medicaments useful for the treatment of tumors. The compounds of the invention will thus be present in pharmaceutical compositions containing compounds of formula I as active ingredients, in admixture with pharmaceutically acceptable vehicles and excipients, which includes any pharmaceutical agent that does not itself induce the production of antibodies harmful to the individual receiving the composition, and which may be administered without undue toxicity. Pharmaceutically acceptable carriers include, but are not limited to, liquids such as water, saline, glycerol and ethanol, and the like, including carriers useful in forming sprays for nasal and other respiratory tract delivery or for delivery to the ophthalmic system. A thorough discussion of pharmaceutically acceptable carriers, diluents, and other excipients is presented in REMINGTON'S PHARMACEUTICAL SCIENCES (Mack Pub. Co., N.J. current edition). Use of such carriers is well known to those skilled in the art and will not be discussed further herein.

Also in accordance with the foregoing, the present invention relates to a method for preventing or treating a disease associated with a change in levels of expression of particular sets of genes in a mammal comprising administering to said mammal an effective amount of a compound of the invention.

In another aspect, the present invention relates to a method for preventing or treating a disorder modulated by altered gene expression, wherein the disorder is selected from the group consisting of cancer, cardiovascular disorders, arthritis, osteoporosis, inflammation, periodontal

disease and skin disorders, comprising administering to a mammal in need of such treatment or prevention a therapeutically effective amount of a compound of the invention.

In a preferred embodiment thereof, the disorder is cancer, more preferably colon cancer, most preferably adenocarcinoma, and the treatment prevents, arrests or reverts tumor growth, metastasis or both.

The compounds of the invention will commonly exert a therapeutic effect by modulation of one or more genes found in a cell, especially a mammalian cell, such as a cancer cell, preferably colon cancer and most preferably adenocarcinoma. Thus, a compound, or compounds, of the invention can be used to determine or demarcate a set of genes by determining modulation of such set of genes by one or more compounds of the invention. For example, where a set of genes is found to be up-regulated in cancer cells versus otherwise normal cells, especially normal cells of the same tissue or organ as the cancer cells, a set of genes can be determined by their common property of being modulated (based on a change in expression of the genes, such as a change in rate or amount of RNA transcribed or the amount of polypeptide produced by said expression) by contacting such genes, or a cell containing such genes, with one or more of the compounds of the invention. The extent of such modulation may, of course, be related to the amount of said compound, or compounds, used in the contacting. Such modulation may include the increased expression of all the determined genes (i.e., the genes of the set), the decreased expression of all genes of the set, or the increase in expression of some of the genes of the set and decreased expression of others. Thus, a gene not modulated by the test compound (the compound used in contacting the genes or cell containing them) is not considered a member of the set.

Thus, the present invention relates to a gene set wherein expression of each member of said gene set is modulated as a result of contacting said

gene set with a compound of the invention. In specific embodiments, expression of each member of said gene set is increased as a result of said contacting or is decreased as a result of said contacting. In another preferred embodiment, the gene set is present in a cell. Such a gene set will commonly be related to a specific disease process, such as a set of genes all of which are modulated by a compound of the invention wherein such compound has a specific therapeutic effect, such as being an anti-neoplastic agent.

In another aspect, the present invention relates to a method for identifying an agent that modulates the expression of a gene set of the invention, comprising:

(a) contacting, or otherwise using, a compound, such as a test compound, a test system, such as a source of genes or polynucleotides, for example, those found to be related to a given disease or disorder, or a set that is modulated by a given compound, or group of compounds, especially where these are found in a cell, so that the cell represents the test system, containing one or more polynucleotides corresponding to each of the members of the gene set of the invention under conditions wherein the members of said gene set are being expressed;

(b) determining a change in expression of each of said one or more polynucleotides of step (a) as a result of said treatment;

wherein said change in expression of step (b) indicates modulation of the members of said gene set by the test compound thereby identifying a test compound that modulates the expression of said gene set.

In one embodiment, the cell is a naturally derived cell that contains genes of a gene set or may be a recombinant cell engineered to comprise the genes or polynucleotides of the gene set. In an alternative embodiment, the test system may comprise the genes or polynucleotides in a cell-free system.

In a related aspect, the present invention provides a method for identifying a test compound that modulates the expression of a gene set, such as a gene set of the invention, comprising:

(a) contacting a test compound with one or more polynucleotides corresponding to each of the members of the gene set of the invention under conditions wherein the members of said gene set are being expressed;

(b) determining a change in expression of each of said one or more polynucleotides of step (a) as a result of said contacting;

wherein said change in expression of step (b) indicates modulation of the members of said gene set thereby identifying a test compound that modulates the expression of said gene set.

As used herein, "corresponding genes" or "corresponding polynucleotides" or "polynucleotides corresponding to genes" refers to polynucleotides and/or genes that encode an RNA that is at least 90% identical, preferably at least 95% identical, most preferably at least 98% identical, and especially identical, to an RNA encoded by one of the genes disclosed herein in Table 19. Such genes will also encode the same polypeptide sequence, but may include differences in such amino acid sequences where such differences are limited to conservative amino acid substitutions, such as where the same overall three dimensional structure, is maintained. A "corresponding gene" includes splice variants thereof.

Because a polynucleotide or gene used in the methods of the invention "corresponds to" a gene present in one of the gene sets of the invention, such as genes identified in Table 19, such polynucleotide or gene encodes an RNA (processed or unprocessed, including naturally occurring splice variants and alleles) that is at least 90% identical, preferably at least 95% identical, most preferably at least 98% identical to, and especially identical to, an RNA that would be encoded by, or be complementary to, such as by hybridization with, a gene of Table 19, or genes of any gene set identified according to the invention. Polynucleotides encoding the same proteins as any of these genes,

regardless of the percent identity of the sequences of such genes and/or polynucleotides, are also specifically contemplated by any of the methods of the present invention. The polynucleotides used in the methods of the invention also include any open reading frames, as defined herein, present therein. As used herein, the term "open reading frame" (or ORF) means a series of triplets coding for amino acids without any termination codons and is a sequence (potentially) translatable into protein.

The polynucleotides useful in the methods of the invention may be genomic in nature and thus represent the sequence of an actual gene, such as a human gene, or may be a cDNA sequence derived from a messenger RNA (mRNA) and thus represent contiguous exonic sequences derived from a corresponding genomic sequence, or they may be wholly synthetic in origin for purposes of practicing the processes of the invention. Because of the processing that may take place in transforming the initial RNA transcript into the final mRNA, the sequences disclosed herein may represent less than the full genomic sequence. They may also represent sequences derived from ribosomal and transfer RNAs. Consequently, the gene as present in the cell (and representing the genomic sequence) and the polynucleotide transcripts disclosed herein, including cDNA sequences, may be identical or may be such that the cDNAs contain less than the full genomic sequence. Such genes and cDNA sequences are still considered "corresponding sequences" (as defined elsewhere herein) because they both encode the same or related RNA sequences (i.e., related in the sense of being splice variants or RNAs at different stages of processing). Thus, by way of non-limiting example only, a gene that encodes an RNA transcript, which is then processed into a shorter mRNA, is deemed to encode both such RNAs and therefore encodes an RNA complementary to (using the usual Watson-Crick complementarity rules), or that would otherwise be encoded by, a cDNA (for example, a sequence as disclosed herein). Thus, the sequences disclosed herein correspond to genes contained in the cancerous cells (here, breast cancer) and are used to determine gene activity or expression because they represent the same

sequence or are complementary to RNAs encoded by the gene. Such a gene also includes different alleles and splice variants that may occur in the cells used in the methods of the invention, such as where recombinant cells are used to assay for anti-neoplastic agents and such cells have been engineered to express a polynucleotide as disclosed herein, including cells that have been engineered to express such polynucleotides at a higher level than is found in non-engineered cancerous cells or where such recombinant cells express such polynucleotides only after having been engineered to do so. Such engineering includes genetic engineering, such as where one or more of the polynucleotides disclosed herein has been inserted into the genome of such cell or is present in a vector.

Such cells, especially mammalian cells, may also be engineered to express on their surfaces one or more of the polypeptides of the invention for testing with antibodies or other agents capable of masking such polypeptides and thereby removing the cancerous nature of the cell. Such engineering includes both genetic engineering, where the genetic complement of the cells is engineered to express the polypeptide, as well as non-genetic engineering, whereby the cell has been physically manipulated to incorporate a polypeptide of the invention in its plasma membrane, such as by direct insertion using chemical and/or other agents to achieve this result.

In a preferred embodiment of such method, the determined change in expression is a decrease in expression of said one or more polynucleotides or a decrease in said expression. In other preferred embodiments, the determined change in expression is a change in transcription of said one or more polynucleotides or a change in activity of a polypeptide, or expression product, encoded by said polynucleotide, including a change in the amount of said polypeptide synthesized, such as by a cell. The term "expression product" means that polypeptide or protein that is the natural translation product of the gene and any nucleic acid sequence coding equivalents resulting from genetic code degeneracy and thus coding for the same amino acid(s).

In additional preferred embodiments, said one or more polynucleotides are present in a cell, preferably a cancer cell, more preferably a colon and breast cancer cell, and most preferably where the coloncancer cell is an adenocarcinoma cancer cell. In another preferred embodiment of the invention, the cell is a recombinant cell engineered to contain said set of genes.

Such methods serve to identify other compounds that have like activity, including expected therapeutic activity, as the compounds of the invention and thus serve as the basis for large scale screening assays for therapeutic compounds. As a result, one or more compounds of the invention can be utilized to determine the presents of gene sets and subsets within the genome of a cell. Thus, the set of all genes modulated by a group of structurally related compounds of the invention can form a gene set while the different sets of genes regulated by each compound of a group will form a subset. By way of non-limiting example, where a structurally related group of 5 of the compounds of the invention (all having generally the structure of Formula I) modulate (by increasing or decreasing) expression of determined genes 1-20, this latter group of genes forms a gene set. Further examination then determines that genes 1-6 are modulated by compound A, genes 7-10 are modulated by compound B, genes 2-4 and 9-12 are modulated by compound C, genes 10-20 are modulated by compound D and the even numbered genes are modulated by compound E. Each of these groups of genes, such as the genes modulated by compound C, is considered a subset of the gene set of genes 1-20. In an analogous manner, the genes modulated by compound E can be themselves further subdivided into at least 2 subsets wherein one subset is made up of the genes whose expression is increased by compound E while the other subset is made up of genes whose expression is decreased by compound E, thus yielding subsets of subsets. It should be noted that within the context of the present invention, it is not necessary to identify subsets and that each so-called subset is, in its own right, a gene set

as used in the invention. The identification of sets and subsets is thus a function of the extent that a user of the methods of the invention wishes to determine modulation of genes resulting from contacting of one or more compounds of the invention. Thus, the genes modulated by a single compound form a gene set and it is not necessary, in carrying out the methods of the invention, to compare different groups of genes for modulation by more than one compound but this may, of course, be done.

In accordance with the foregoing, the present invention relates to a set of genes comprising a plurality of subsets of genes wherein each subset of said plurality is a gene set identified by the methods of the invention. The present invention also relates to compounds identified as having activity using the methods of the invention, such as novel compounds not specifically described herein by structure but which have been identified by their ability to modulates one or more gene sets modulated by compounds of the invention.

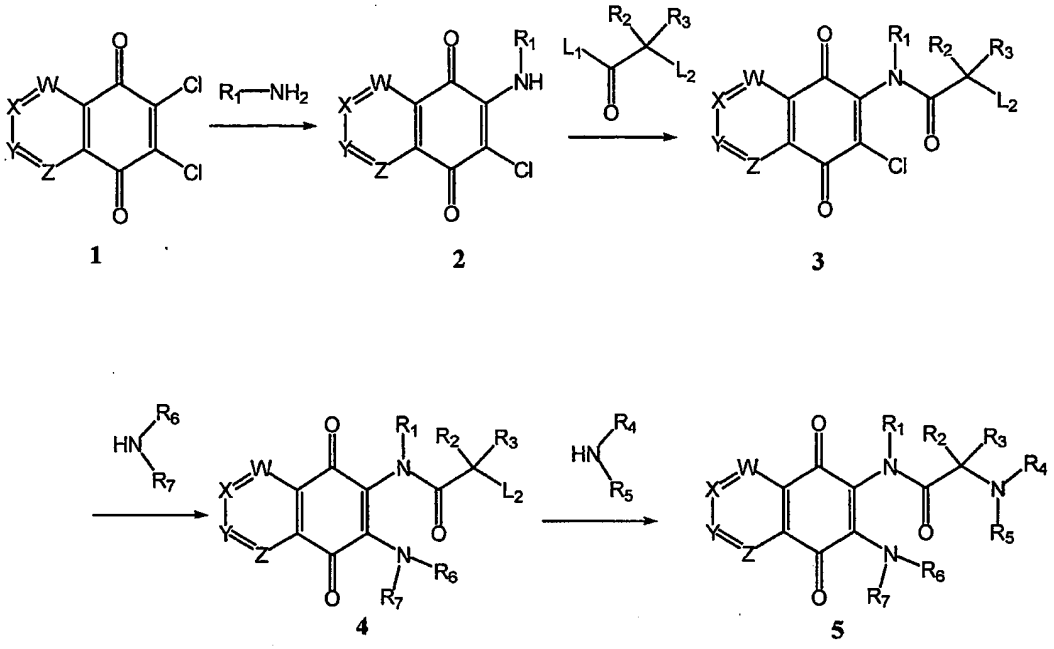
In a preferred embodiment, the present invention encompasses the gene sets and subsets of the genes identified in Table 19.

The present invention comprises also processes for the preparation of compounds of formula I, and the relative key intermediates.

Compound Preparation:

The compounds of the invention can be prepared using a variety of procedures known in the art. The starting materials used in preparing the compounds of the invention are known, made by known methods, or are commercially available. Particularly preferred syntheses are described in the following general reaction schemes.

Scheme 1:



The dichloro compound **1** is either commercially available or can be synthesized using methods known in the literature.

1. Shaikh I. A. et al, J. Med. Chem, 29(8), 1329-1340, (1986)
2. Vlderrama el al, Syn. Comm., 27(12), 2143-2157, (1997)
3. Chu, Kwong-Yung; et al. Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1978)
4. Matsuhisa A. et al, Patent WO 01/60803 A1

The compound **1** is reacted with an amine in an appropriate solvent to provide the corresponding derivative 2. The compound **2** is then reacted with an appropriate 2-halo, 2-substituted acetyl halide to obtain the corresponding 3 derivatives. A reaction of crude or purified compound **3** with an amine gives compound **4**. Compound **4** with or without isolation is treated with an amine in a suitable solvent at an appropriate temperature to afford compound **5**.

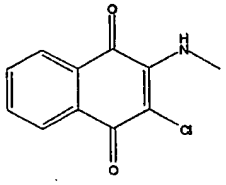
In the same way, independent and selective modification of R_1, R_2, R_3, R_4, R_5, R_6, and R_7 using methods known in the literature readily affords additional compounds of formula I. Thus, compounds for which no separate preparation is provided herein are made by methods known in the literature or are of common knowledge to the skilled artisan.

The skilled artisan will recognize that some reactions are best carried out when another potentially reactive functionality on the molecule is masked or protected, thus avoiding any undesirable side reactions and/or increasing the yield of the reaction. Often protecting groups are used to accomplish such increased yields or to avoid the undesired reactions. Such reactions are well within the ability of the skilled artisan. Some examples are found in T. Greene, Protecting Groups in Organic Synthesis.

In addition, it is to be appreciated that one optical isomer may have favorable properties over the other and thus the disclosure of a racemic mixture within the present invention may also include either optically active isomer if such isomer has advantageous physiological activity in accordance with the methods of the invention.

Example-A1

2-Chloro-3-methylamino-[1,4]naphthoquinone



To a solution of 22.7g (100mmol, 1equivalent) of 2,3-dichloro-[1,4]naphthoquinone in 350 ml of anhydrous THF was added 200ml of 2.0M methyl amine in THF (200mmol, 2 equivalents). To the mixture was added 34 ml of N, N-diisopropylethylamine (200mmol, 2 equivalents) and it was shaken at room temperature for overnight (16-20 hours).

The red precipitates formed were filtered and washed with ether. The residue was again washed with water and ether. The solid was dried under vacuum. The filtrate was checked for the desired product, and then THF was evaporated. The residue was recrystallized with dichloromethane/ether. The titled compound was collected as a red solid (18g, Yield 74%).

In a process analogous to Example A1 using appropriate starting materials, the corresponding compounds are prepared as follows:

Example	Chemical Name
A2	(3-Chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-ylamino)-acetic acid tert-butyl ester
A3	2-(1-Benzyl-piperidin-4-ylamino)-3-chloro-[1,4]naphthoquinone
A4	2-(3-Chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-ylamino)-3-phenyl-propionic acid tert-butyl ester
A5	2-(4-Acetyl-phenylamino)-3-chloro-[1,4]naphthoquinone
A6	2,6-Dichloro-5,8-dihydroxy-3-(3-{4-[3-(6-oxo-6H-2,10b-diaza-aceanthrylen-5-ylamino)-propyl]-piperazin-1-yl}-propylamino)-[1,4]naphthoquinone
A7	2-Chloro-3-(2-pyridin-4-yl-ethylamino)-[1,4]naphthoquinone
A8	2-Chloro-3-(3-{4-[3-(6-oxo-6H-2,10b-diaza-aceanthrylen-5-ylamino)-propyl]-piperazin-1-yl}-propylamino)-[1,4]naphthoquinone
A9	2-Chloro-3-(3-morpholin-4-yl-propylamino)-[1,4]naphthoquinone
A10	2-Chloro-3-(4-dimethylamino-benzylamino)-[1,4]naphthoquinone
A11	2-Chloro-3-(4-dimethylamino-phenylamino)-[1,4]naphthoquinone
A12	2-Chloro-3-[(1-ethyl-pyrrolidin-2-ylmethyl)-amino]-[1,4]naphthoquinone
A13	2-Chloro-3-[2-(1,2,2,6,6-pentamethyl-piperidin-4-yl)-ethylamino]-[1,4]naphthoquinone
A14	2-Chloro-3-[3-(2-oxo-pyrrolidin-1-yl)-propylamino]-[1,4]naphthoquinone
A15	2-Chloro-3-[3-(methyl-phenyl-amino)-propylamino]-[1,4]naphthoquinone
A16	2-Chloro-3-{[(4-methyl-pyridin-2-yl)-phenyl-methyl]-amino}-[1,4]naphthoquinone
A17	2-Chloro-3-phenylamino-[1,4]naphthoquinone
A18	2-Chloro-5,8-dihydroxy-3-(3-{4-[3-(6-oxo-6H-2,10b-diaza-aceanthrylen-5-ylamino)-propyl]-piperazin-1-yl}-propylamino)-[1,4]naphthoquinone
A19	4-(3-Chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-ylamino)-benzoic acid ethyl ester

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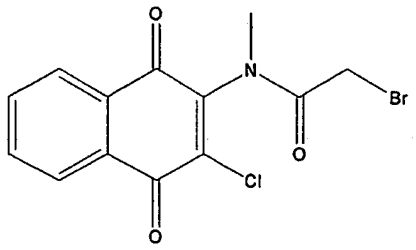
Example-B1

2-Bromo-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide



To a solution of 8g of 2-chloro-3-methylamino-[1,4]naphthoquinone (36mmol) in 400 ml 1,4-dioxane was added 10g of potassium carbonate (72mmol). The mixture was heated until the starting material was completely dissolved. To the solution, 12.5ml of bromoacetyl bromide (144mmol) was added and refluxed for 1 hour. Inorganic materials were filtered and washed thoroughly with dichloromethane. The filtrate was evaporated and the residue was purified by flash silica gel column using 75:25- hexanes: ethyl acetate. The compound was collected as yellow oil. (10g, Yield 80%).

In a process analogous to Example B1 using appropriate 2-chloro-3-substituted amino [1,4] naphthoquinone (Example A) and corresponding acid bromide following compounds are prepared.

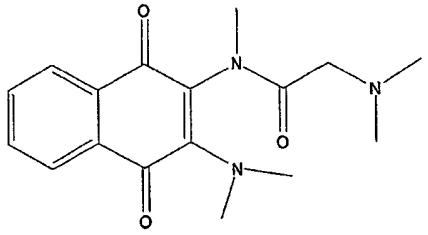
2-Bromo-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-acetamide

2-Bromo-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide

2-Bromo-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-propionamide

Example 1 (Compound 1, Table 1)

2-Dimethylamino-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide



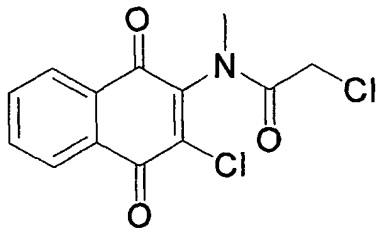
To a solution of 2.5g of 2-bromo-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide (7mmol, 1equivalent) in 200ml of ethyl acetate was added 28 ml of 2.0M dimethylamine solution in tetrahydrofuran (56mmol, 8 equivalents). The amine solution was added in two portions stirring for 15 min after each addition. The solvent was then evaporated and then sample was purified on a silica gel column using initially ethyl acetate and then 10-20 % methanol in ethyl acetate. The solvent was evaporated and the residue was dissolved in DMSO. It was then purified further on preparative LCMS using 0.1% NH_4OH in water/acetonitrile as mobile phase. (592mg, Yield 26%); H^1 NMR (400MHz, $CDCl_3$) 2.97 (s, 6H), 3.08 (s, 3H), 3.20 (s, 6H), 3.64 (s, 2H), 7.62 (m, 2H), 7.95 (t, 2H).

Compound 2-119 (Table 1)

In a process analogous to Example 1 (Table 1) using appropriate chloro-bromo naphthoquinone (Example B) and the corresponding secondary amine, following compounds are prepared as shown in Table 1 .

Example-C1

2-Chloro-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide



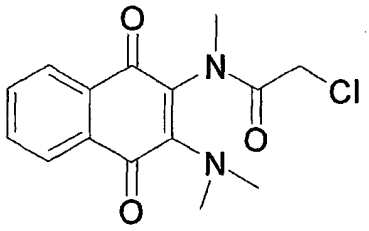
To a solution of 10g of 2-chloro-3-methylamino-[1,4]naphthoquinone (45 mmol) in 250 mL of dioxane was added 172 mL of chloroacetyl chloride (48 equivalents). The reaction was heated at 85° C for 16 hours. The solvent was evaporated and the material was purified on silica gel using DCM and hexanes as solvents. The pure fractions were combined and the solvent was evaporated. The product was collected as a yellow/brown solid. (12.1g, Yield 90%).

In a process analogous to Example C1 using appropriate 2-chloro-3-substituted amino-[1,4]naphthoquinone (Example A) and corresponding acid chloride following compounds are prepared.

Example	Chemical Name
C2	2-Chloro-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-acetamide
C3	2-Chloro-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-propionamide
C4	2-Chloro-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-2-phenyl-acetamide
C5	2-Chloro-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-propionamide
C6	2-Chloro-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-2-phenyl-acetamide

Example D1

2-Chloro-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide



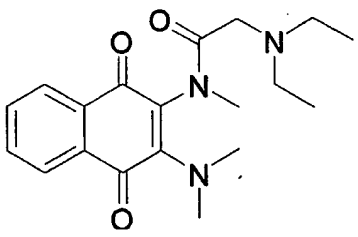
To a solution of 19g of 2-chloro-N-(3-chloro-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide (63 mmol) in 200 mL of ethyl acetate was added slowly 22 mL of N, N-diisopropylethylamine (2 equivalents). 70 mL of 2.0M solution of dimethylamine in terahydrofuran (2.25 equivalents) was diluted with 100 mL of ethyl acetate. This amine solution was added slowly to the reaction mixture over one hour at room temperature. After stirring for an additional hour, the reaction was filtered and the solid material was washed with ethyl acetate. The filtrate was concentrated and purified using a normal phase column chromatography, and ethyl acetate and hexanes as solvents. The pure fractions were combined and the solvent was evaporated. The product was collected as a red solid. (10.1g, Yield- 52%). H^1 NMR (400MHz, CDCl3): 3.09 (s, 3H), 3.23 (s, 6H), 4.01 (q, 2H), 7.65-7.77 (m, 2H), 8.03 (d, 1H), 8.08 (d, 1H).

In a process analogous to Example D1 using appropriate dichloro naphthoquinone derivatives (Example C) and corresponding secondary amine, the following compounds are prepared.

Example	Chemical Name
D2	2-Chloro-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-acetamide
D3	2-Chloro-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-propionamide
D4	2-Chloro-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-2-phenyl-acetamide
D5	2-Chloro-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-propionamide
D6	2-Chloro-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-2-phenyl-acetamide

Example 2 (Compound 1, Table 2)

2-Diethylamino-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide



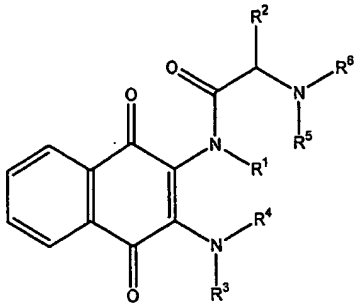
To a solution of 0.54 g of 2-chloro-N-(3-dimethylamino-1,4-dioxo-1,4-dihydro-naphthalen-2-yl)-N-methyl-acetamide (1.8 mmol) in 20 mL of ethyl acetate was added 2.2 mL of ethylamine (21.6mmol, 12 equiv). The mixture was stirred at room temperature for two hours. The reaction mixture was then filtered and the solid was washed with ethyl acetate until all red material was dissolved. The red filtrate was concentrated and purified on a normal phase column chromatography using ethyl acetate. The pure fractions were combined and concentrated. The solid was then dissolved in 20mL of DCM and 12 equiv of 1.0M HCl in diethyl ether was added to produce hydrochloride salt. Organic solvents were evaporated and the product was dissolved in 5.0

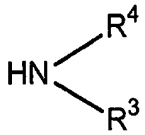
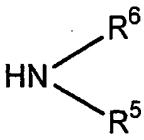
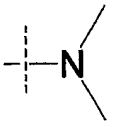
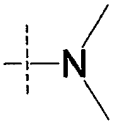
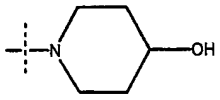
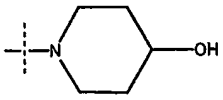
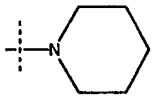
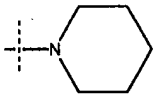
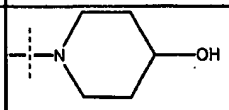
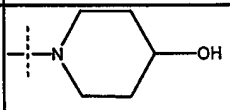
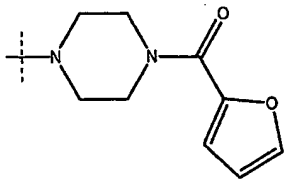
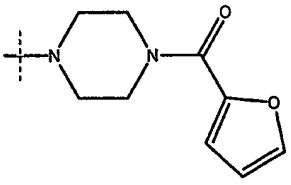
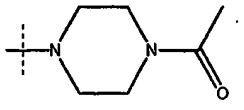
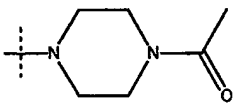
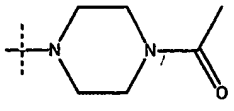
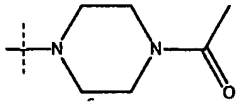
mL of HPLC grade water. This material was freeze dried to give 0.42 g of final product as its hydrochloride salt. (Yield 62%). H^1 NMR (400MHz, DMSO, D2O) 1.14 (t, 6H), 2.97 (s, 3H), 3.08-3.0 (m, 10H), 3.80 (d, 1H), 4.02 (d, 1H), 7.7-7.9 (m, 2H), 7.89-8.0 (m, 2H).

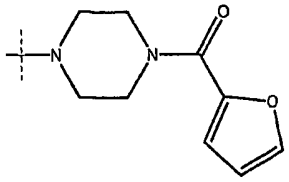
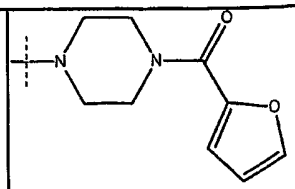
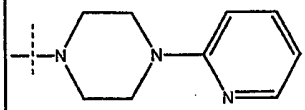
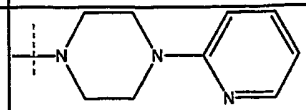
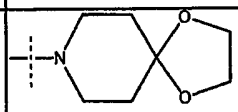
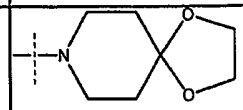
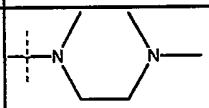
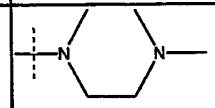
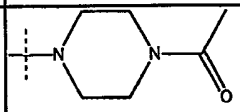
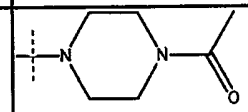
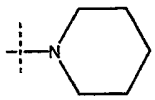
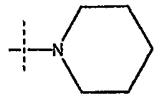
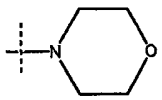
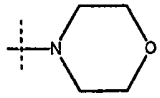
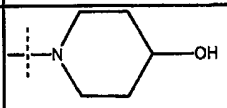
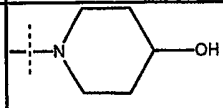
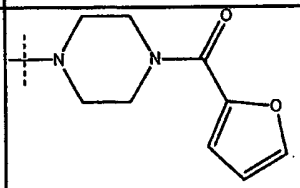
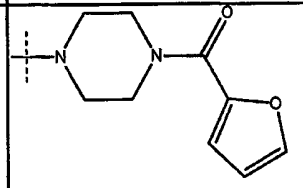
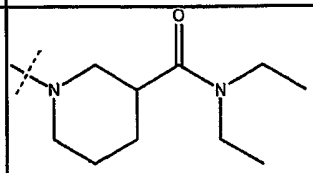
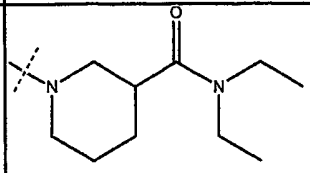
Compounds 2-119 (Table 2)

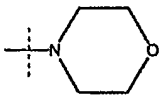
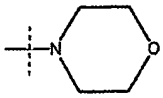
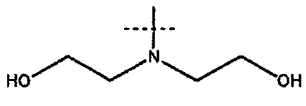
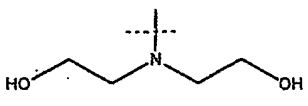
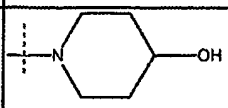
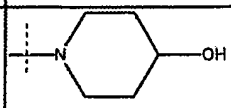
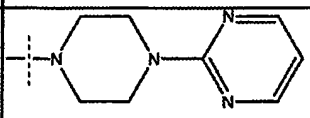
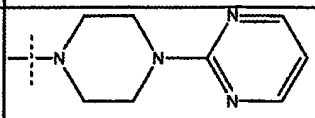
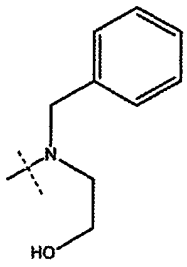
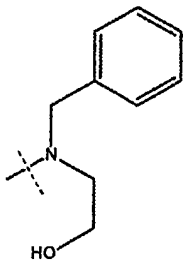
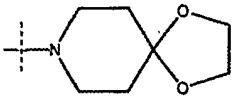
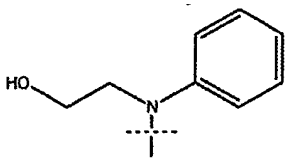
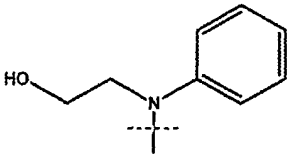
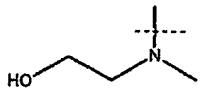
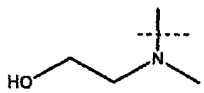
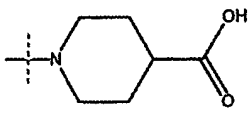
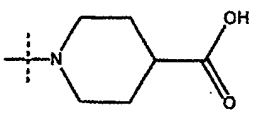
In a process analogous to Example 2 using appropriate chloro naphthoquinone (Example D) and the corresponding secondary amine, compounds are prepared as shown in Table 2.

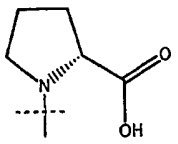
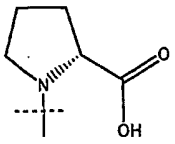
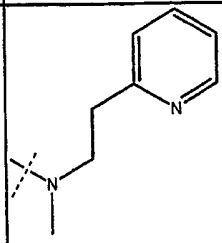
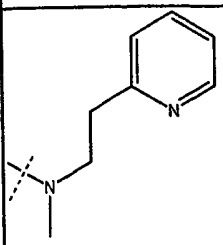
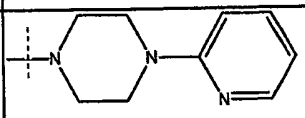
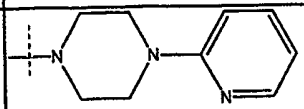
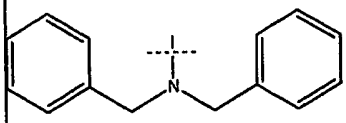
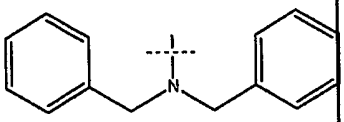
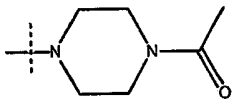
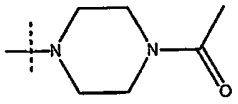
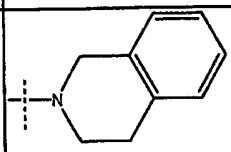
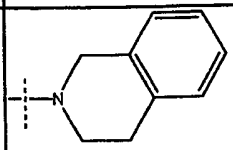
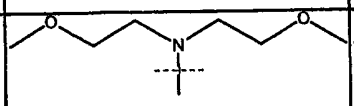
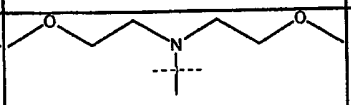
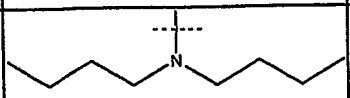
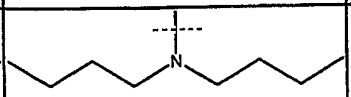
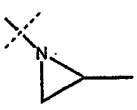
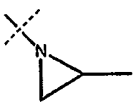
Table 1

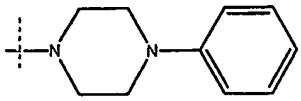
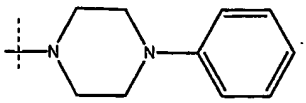
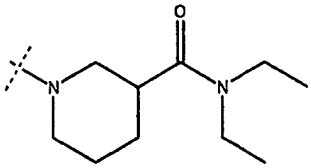
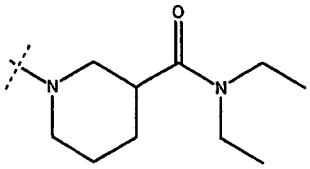
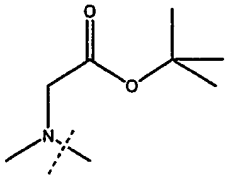
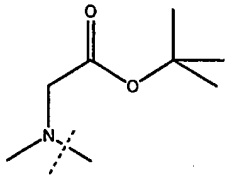
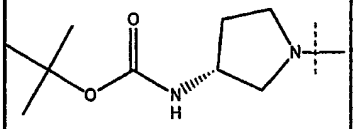
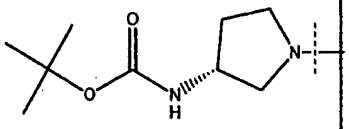
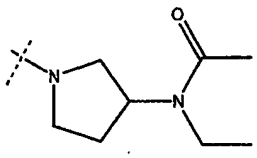
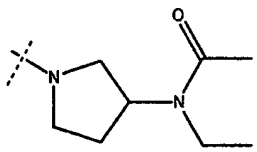
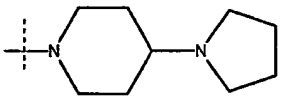
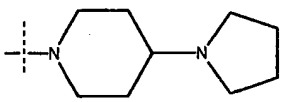
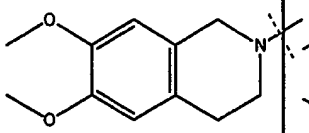
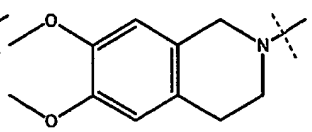


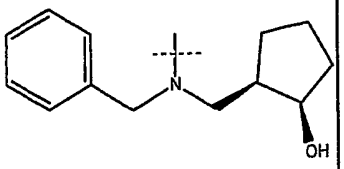
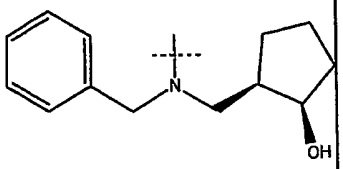
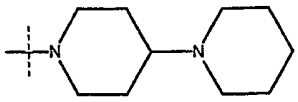
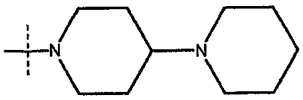
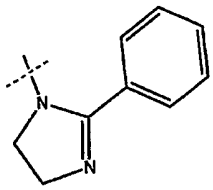
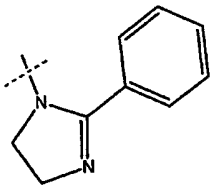
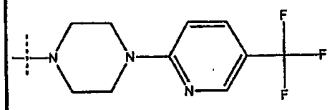
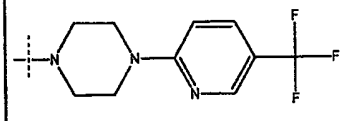
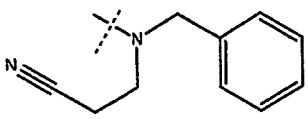
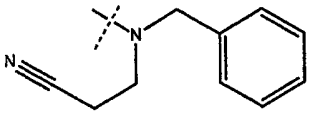
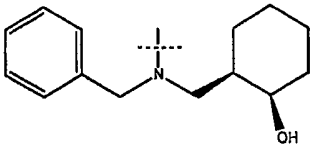
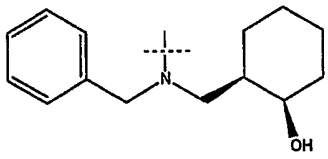
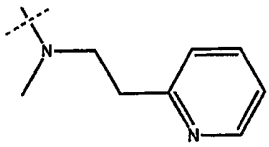
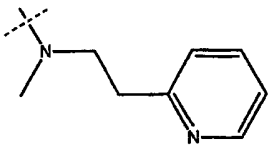
Cmpd	R_1	R_2			MW
1	CH3	H			315.37
2	H	H			413.47
3	H	CH3			395.50
4	H	CH3			427.50
5	H	H			571.59
6	H	H			467.52
7	H	CH3			481.55

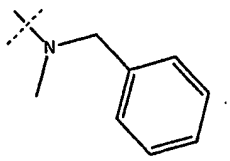
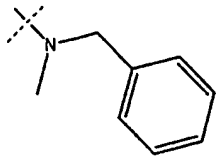
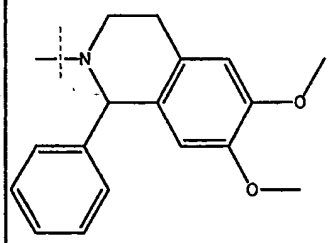
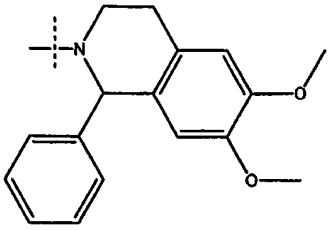
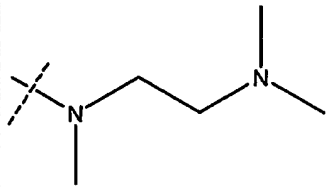
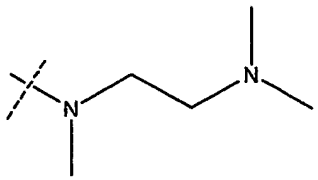
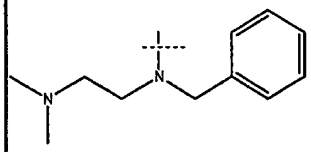
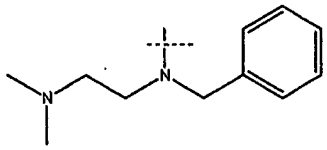
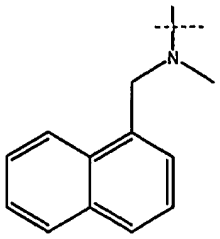
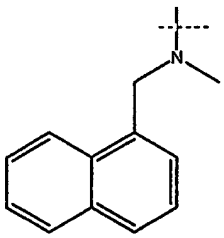
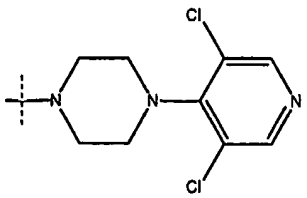
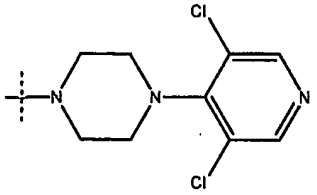
8	H	CH3			585.62
9	CH3	H			551.65
10	CH3	H			511.57
11	CH3	H			429.56
12	CH3	H			481.55
13	CH3	H			395.50
14	CH3	H			399.45
15	CH3	H			427.50
16	CH3	H			585.62
17	CH3	H			593.76

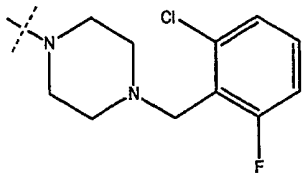
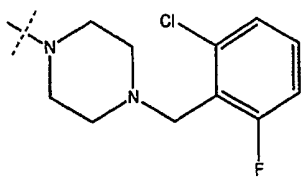
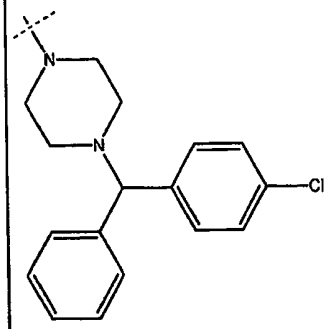
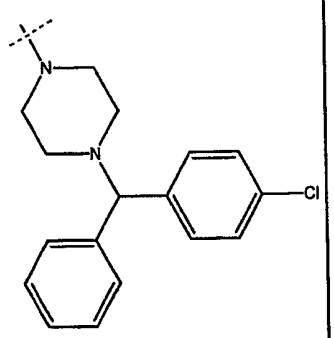
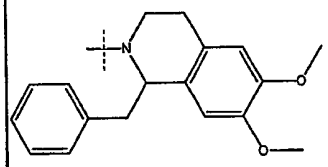
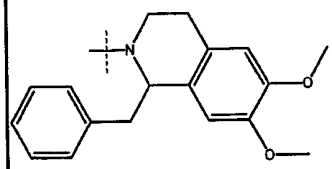
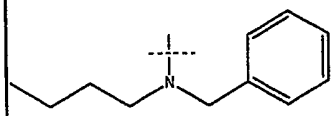
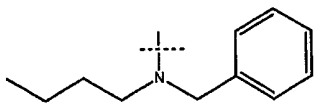
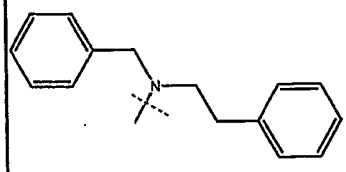
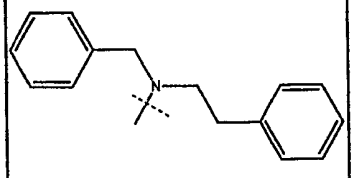
18	CH3	H			399.43
19	CH3	H			435.47
20	CH3	H			427.49
21	CH3	H			553.61
22	CH3	H			527.61
23	CH3	H			511.56
24	CH3	H			499.55
25	CH3	H			375.41
26	CH3	H			483.51

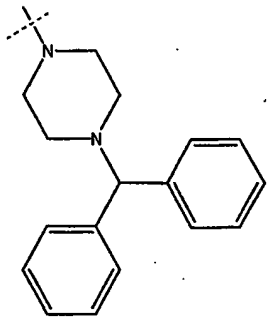
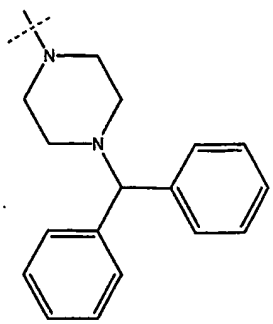
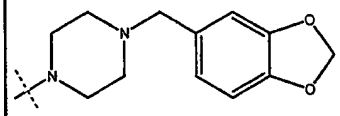
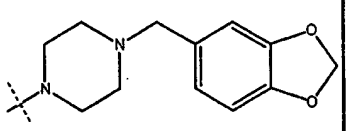
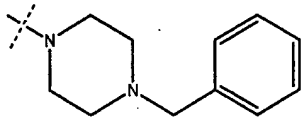
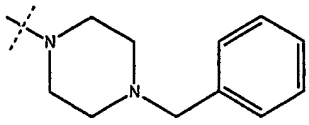
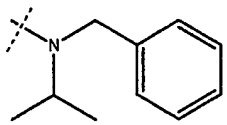
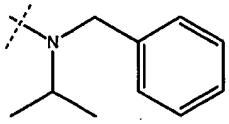
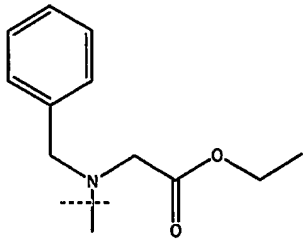
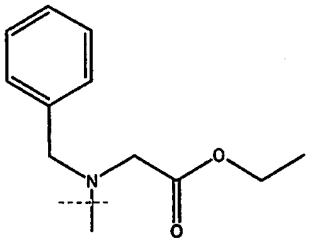
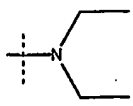
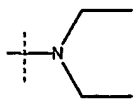
27	CH3	H			455.46
28	CH3	H			497.58
29	CH3	H			551.64
30	CH3	H			619.75
31	CH3	H			481.54
32	CH3	H			491.58
33	CH3	H			491.57
34	CH3	H			483.68
35	CH3	H			339.38

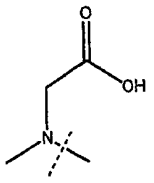
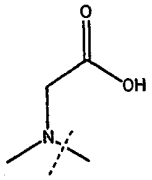
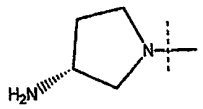
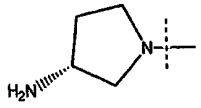
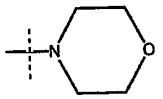
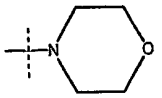
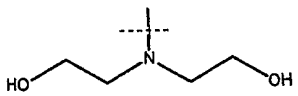
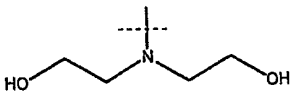
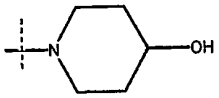
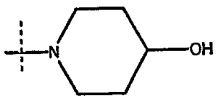
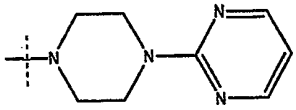
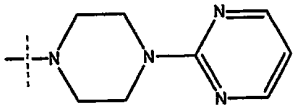
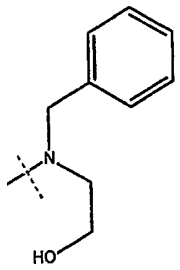
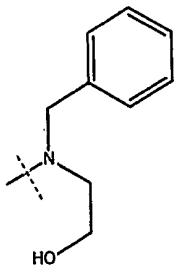
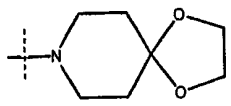
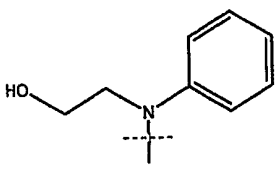
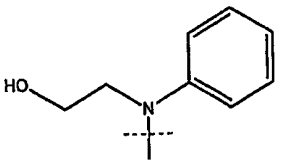
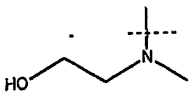
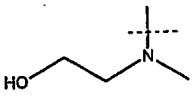
36	CH3	H			549.66
37	CH3	H			593.75
38	CH3	H			515.59
39	CH3	H			597.70
40	CH3	H			537.65
41	CH3	H			533.70
42	CH3	H			611.68

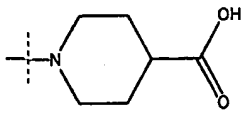
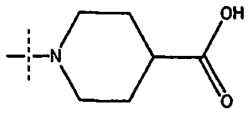
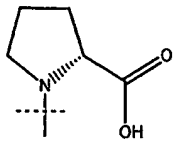
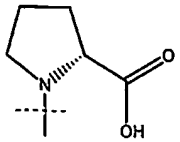
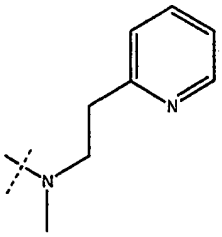
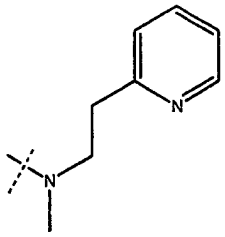
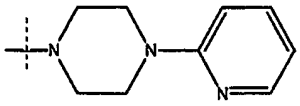
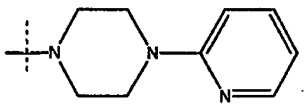
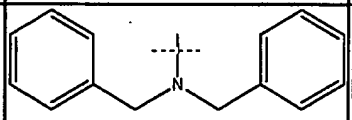
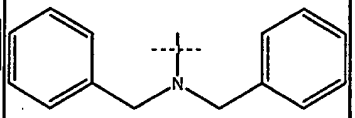
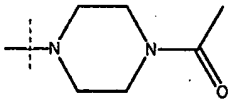
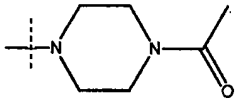
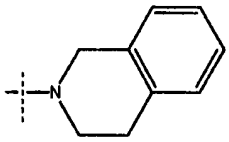
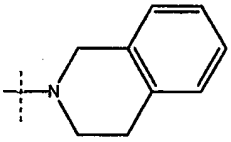
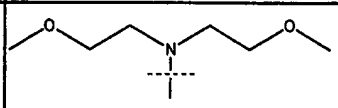
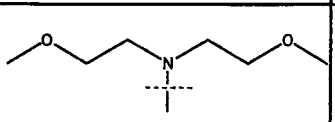
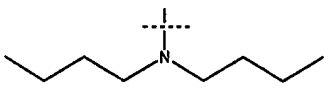
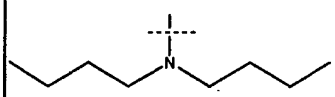
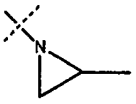
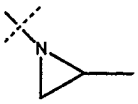
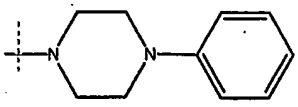
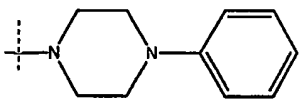
43	CH3	H			635.79
44	CH3	H			561.76
45	CH3	H			517.58
46	CH3	H			687.63
47	CH3	H			545.63
48	CH3	H			663.84
49	CH3	H			497.58

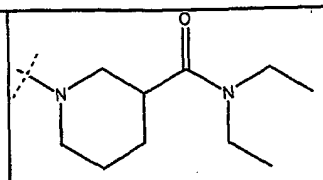
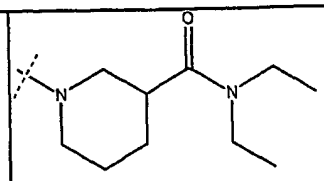
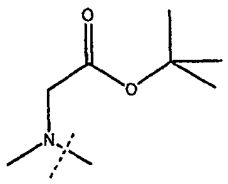
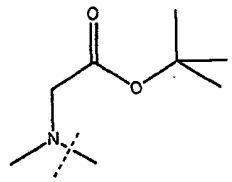
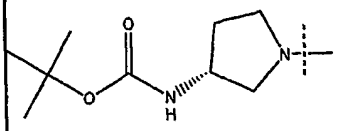
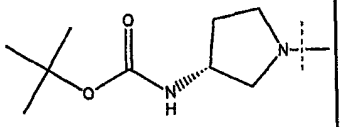
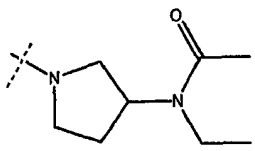
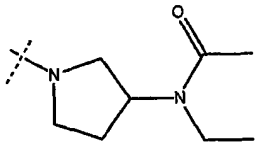
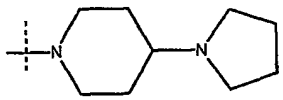
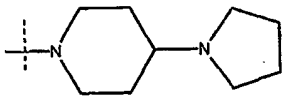
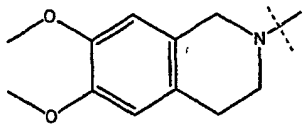
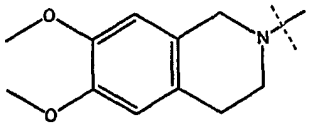
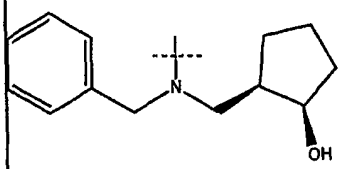
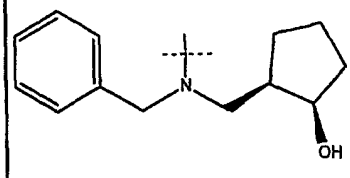
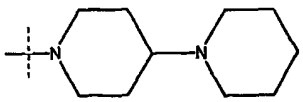
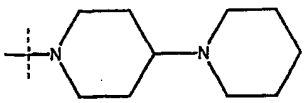
50	CH3	H			467.56
51	CH3	H			763.88
52	CH3	H			429.56
53	CH3	H			581.75
54	CH3	H			567.68
55	CH3	H			689.42

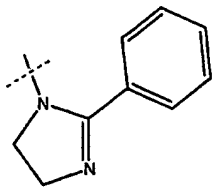
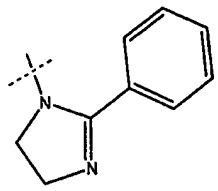
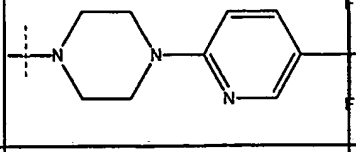
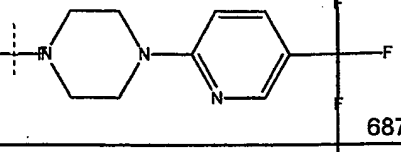
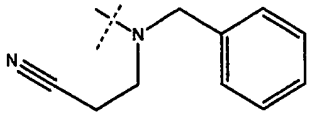
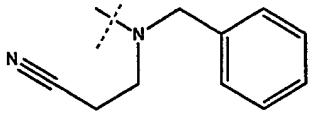
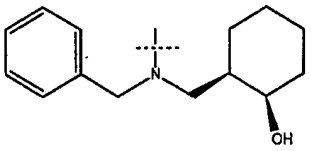
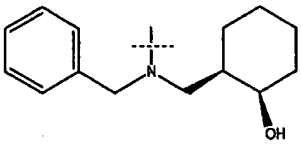
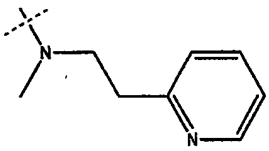
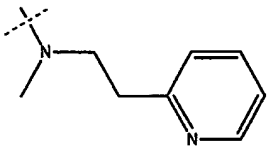
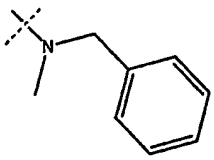
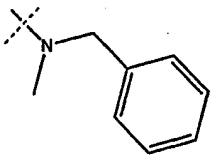
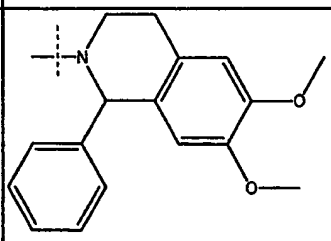
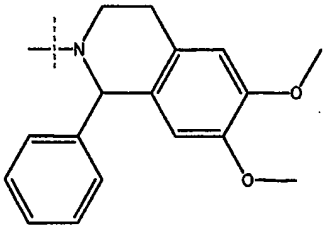
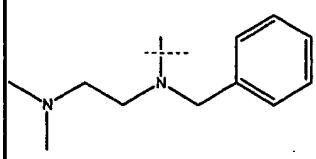
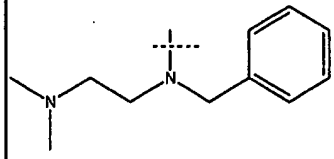
56	CH3	H			682.59
57	CH3	H			798.80
58	CH3	H			791.93
59	CH3	H			551.72
60	CH3	H			647.80

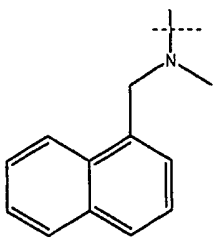
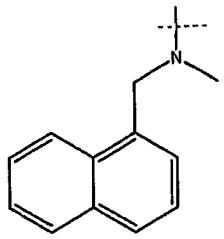
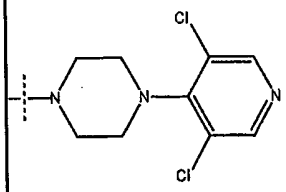
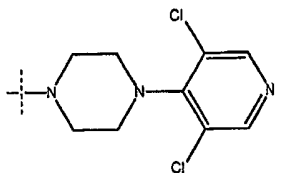
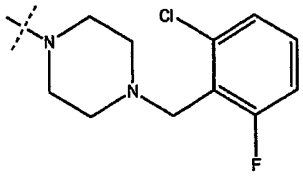
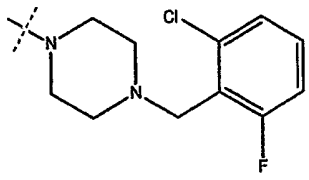
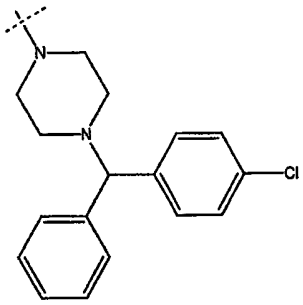
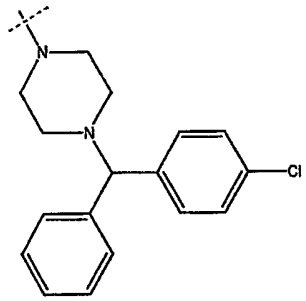
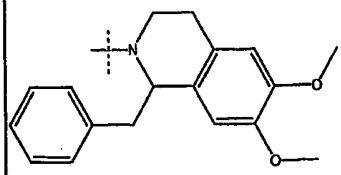
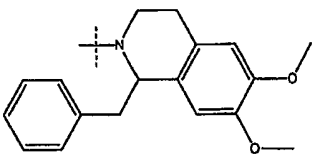
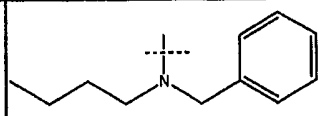
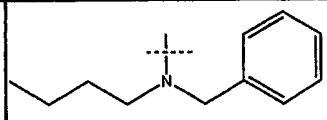
61	CH3	H			729.91
62	CH3	H			665.73
63	CH3	H			577.71
64	CH3	H			523.66
65	CH3	H			611.68
66	CH3	H			371.47

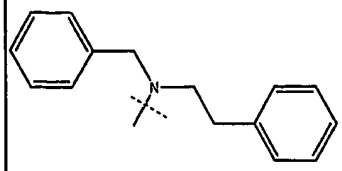
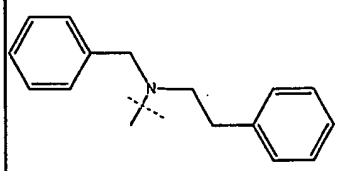
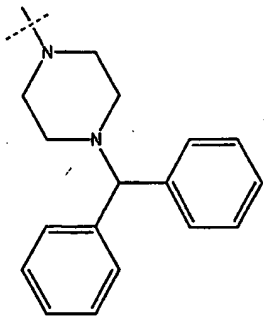
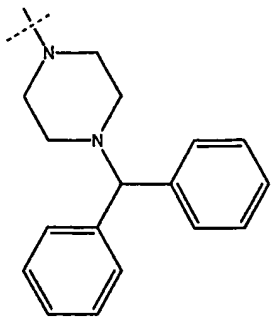
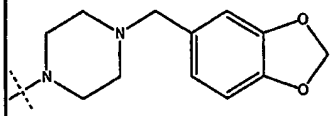
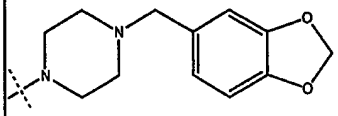
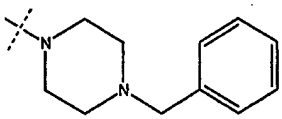
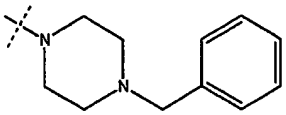
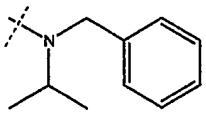
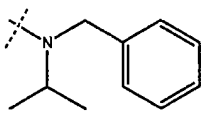
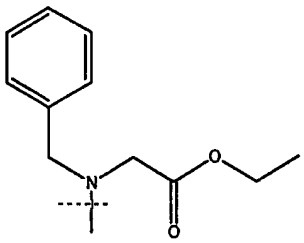
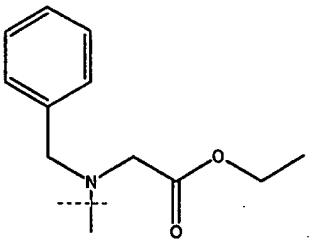
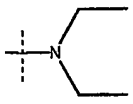
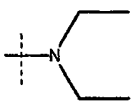
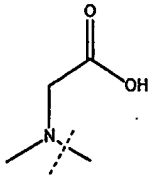
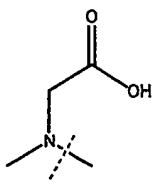
67	CH3	H			403.38
68	CH3	H			397.47
69	H	CH3			399.43
70	H	CH3			435.47
71	H	CH3			427.49
72	H	CH3			553.61
73	H	CH3			527.61
74	H	CH3			511.56
75	H	CH3			499.55
76	H	CH3			375.41

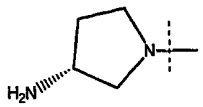
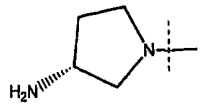
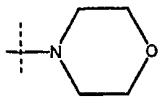
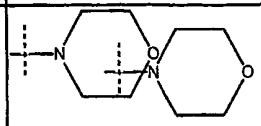
77	H	CH3			483.51
78	H	CH3			455.46
79	H	CH3			497.58
80	H	CH3			551.64
81	H	CH3			619.75
82	H	CH3			481.54
83	H	CH3			491.58
84	H	CH3			491.57
85	H	CH3			483.68
86	H	CH3			339.38
87	H	CH3			549.66

88	H	CH3			593.75
89	H	CH3			515.59
90	H	CH3			597.70
91	H	CH3			537.65
92	H	CH3			533.70
93	H	CH3			611.68
94	H	CH3			635.79
95	H	CH3			561.76

96	H	CH3			517.58
97	H	CH3			687.63
98	H	CH3			545.63
99	H	CH3			663.84
100	H	CH3			497.58
101	H	CH3			467.56
102	H	CH3			763.88
103	H	CH3			581.75

104	H	CH3			567.68
105	H	CH3			689.42
106	H	CH3			682.59
107	H	CH3			798.80
108	H	CH3			791.93
109	H	CH3			551.72

110	H	CH3			647.80
111	H	CH3			729.91
112	H	CH3			665.73
113	H	CH3			577.71
114	H	CH3			523.66
115	H	CH3			611.68
116	H	CH3			371.47
117	H	CH3			403.38

118	H	CH3			397.47
119	H	H			385.42

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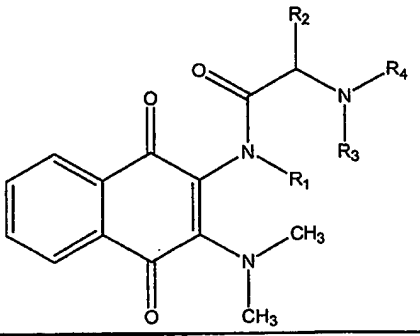
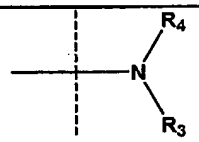
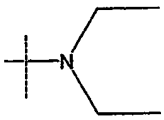
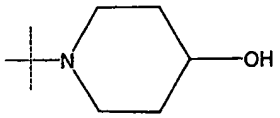
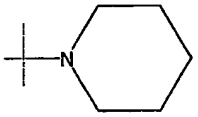
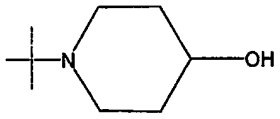
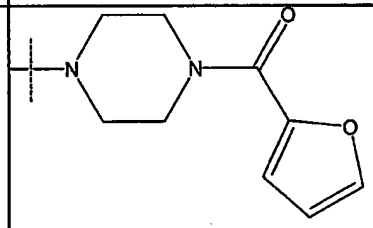
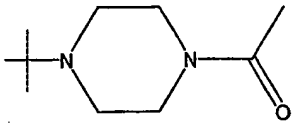
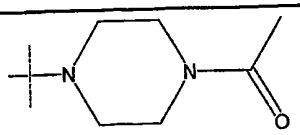
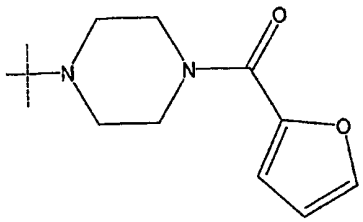
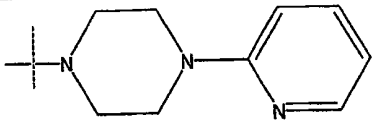
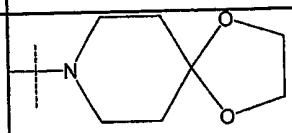
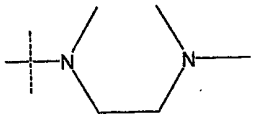
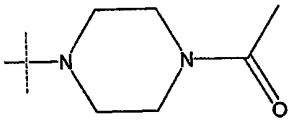
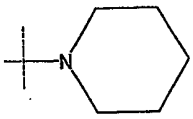
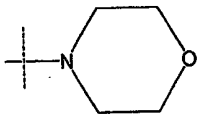
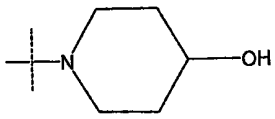
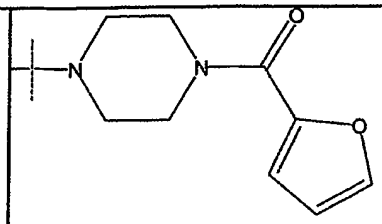
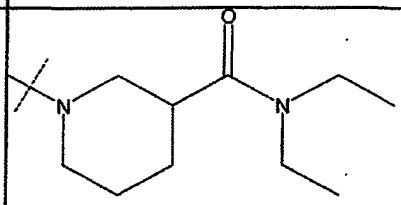
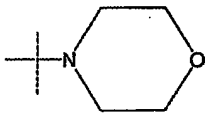
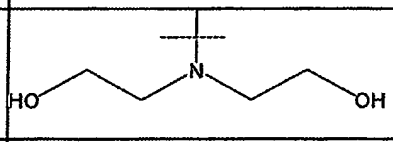
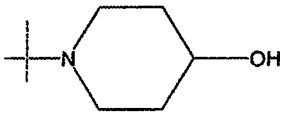
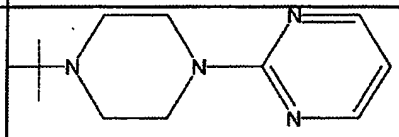
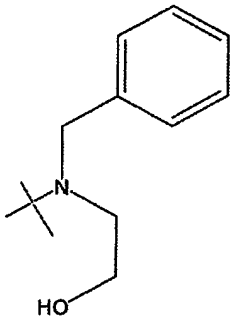
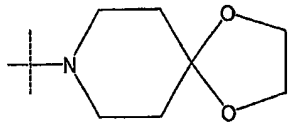
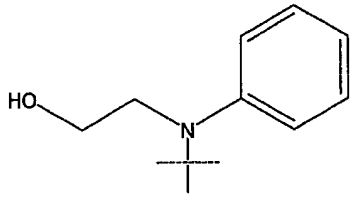
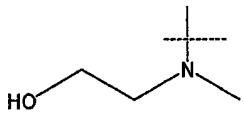
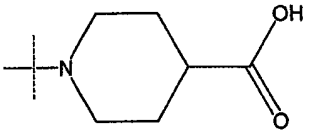
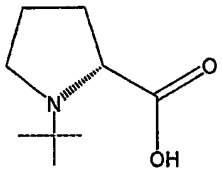
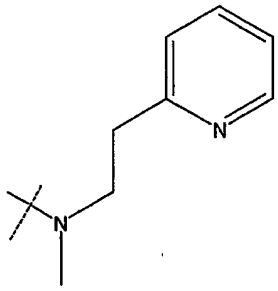
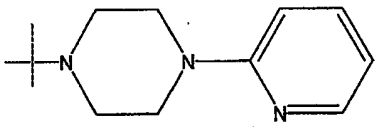
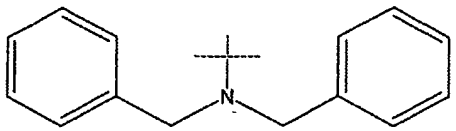
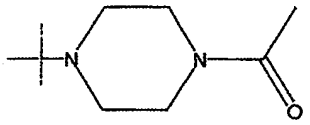
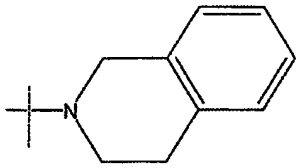
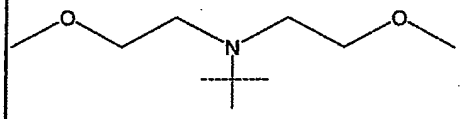
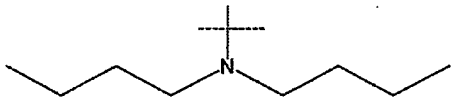
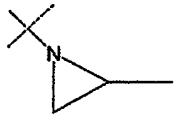
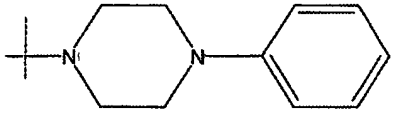
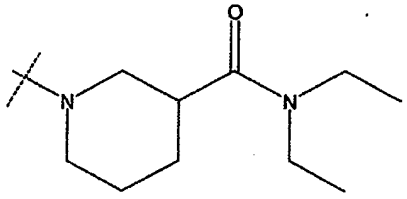


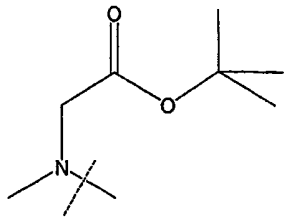
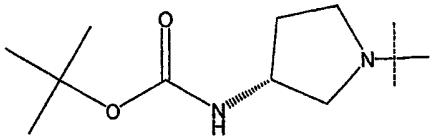
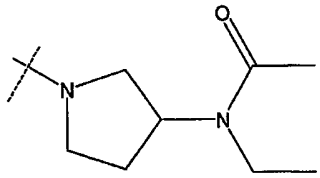
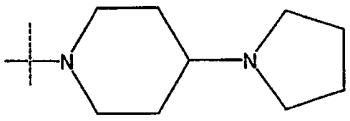
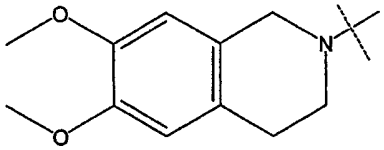
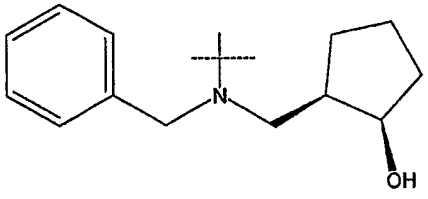
Cmpd	R_1	R_2		MW
1	CH3	H		343.44
2	H	H		357.42
3	H	CH3		355.45
4	H	CH3		371.45
5	H	H		436.48
6	H	H		384.44

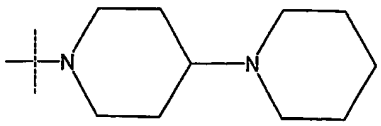
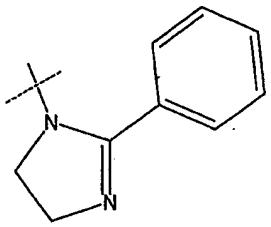
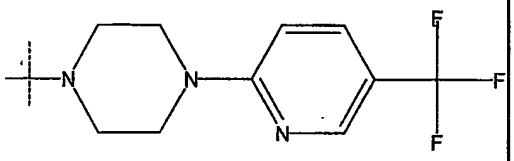
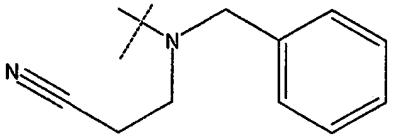
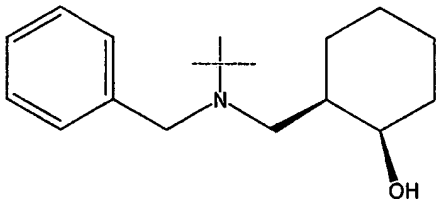
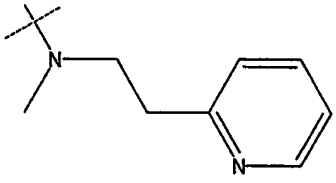
7	H	CH3		398.47
8	H	CH3		450.50
9	CH3	H		433.52
10	CH3	H		413.48
11	CH3	H		372.48
12	CH3	H		398.47
13	CH3	H		355.45
14	CH3	H		357.42
15	CH3	H		371.45

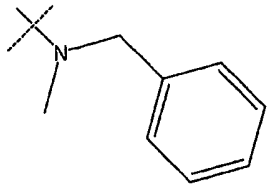
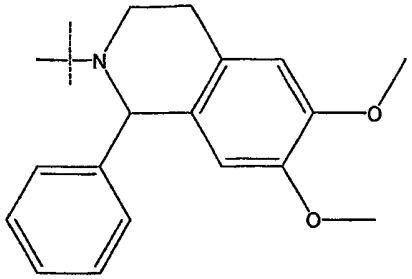
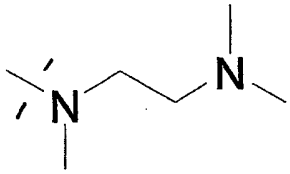
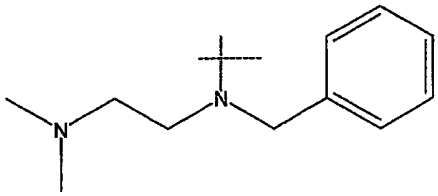
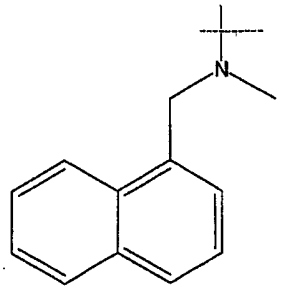
16	CH3	H		450.50
17	CH3	H		454.58
18	CH3	H		357.42
19	CH3	H		375.43
20	CH3	H		371.45
21	CH3	H		434.51
22	CH3	H		421.50

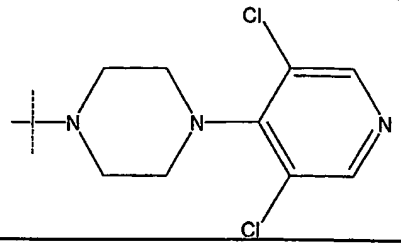
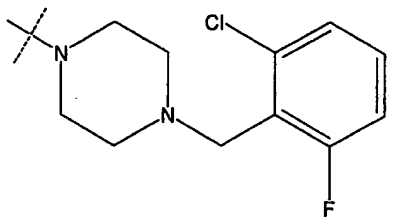
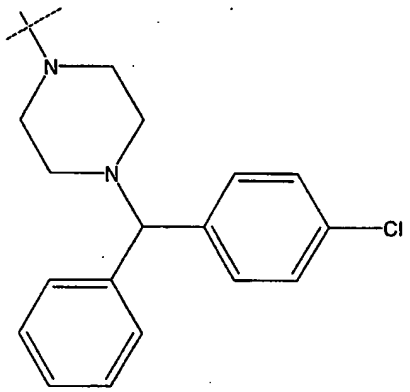
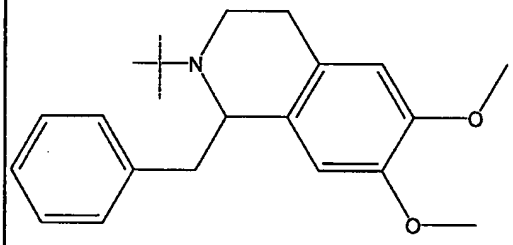
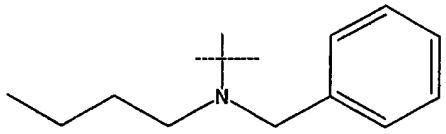
23	CH3	H		413.48
24	CH3	H		407.48
25	CH3	H		345.41
26	CH3	H		399.46
27	CH3	H		385.43
28	CH3	H		406.49
29	CH3	H		433.52

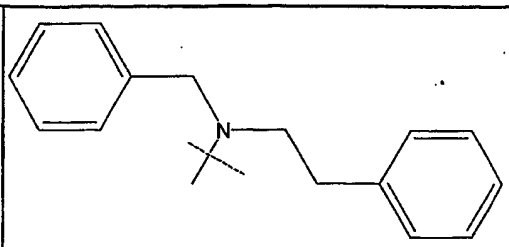
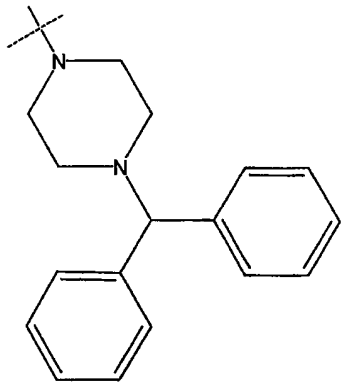
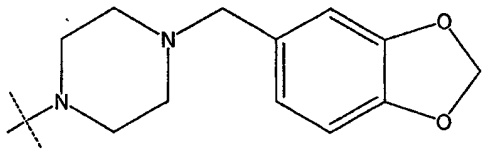
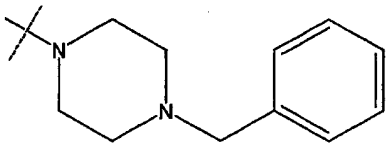
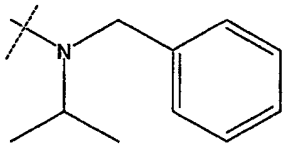
30	CH3	H		467.57
31	CH3	H		398.47
32	CH3	H		403.49
33	CH3	H		403.49
34	CH3	H		399.54
35	CH3	H		327.39
36	CH3	H		432.53
37	CH3	H		454.58

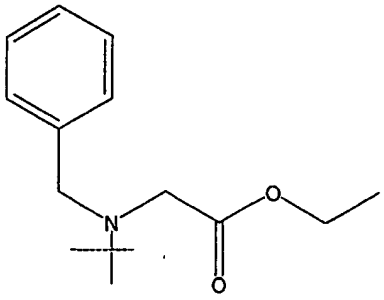
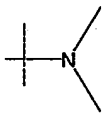
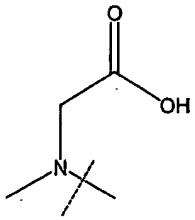
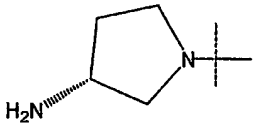
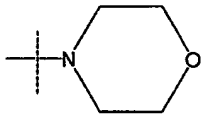
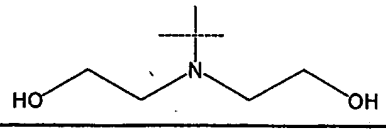
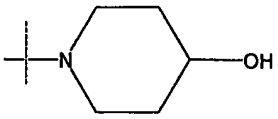
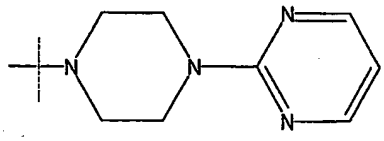
38	CH3	H		415.50
39	CH3	H		456.55
40	CH3	H		426.52
41	CH3	H		424.55
42	CH3	H		463.54
43	CH3	H		475.60

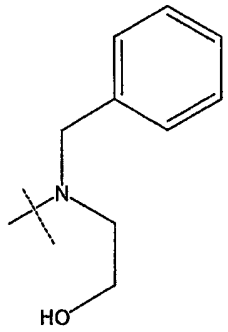
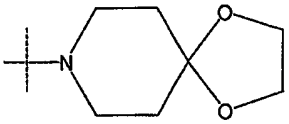
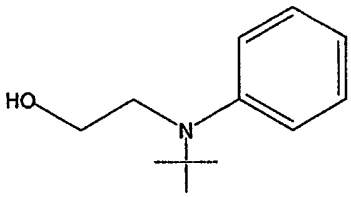
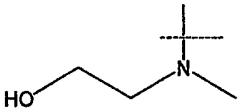
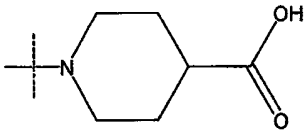
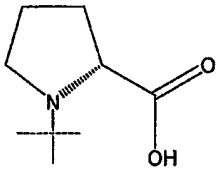
44	CH3	H		438.58
45	CH3	H		416.49
46	CH3	H		501.52
47	CH3	H		430.51
48	CH3	H		489.62
49	CH3	H		406.49

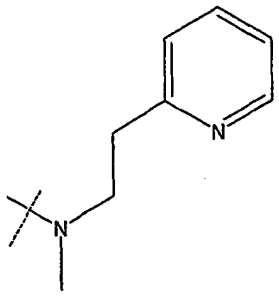
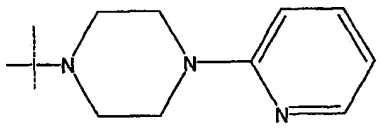
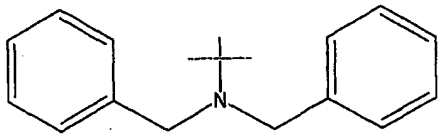
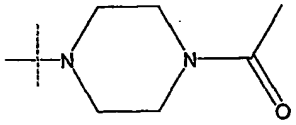
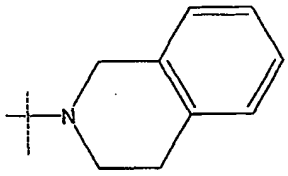
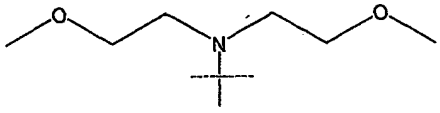
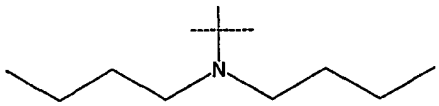
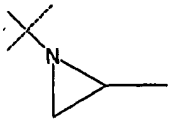
50	CH3	H		391.48
51	CH3	H		539.64
52	CH3	H		372.48
53	CH3	H		448.57
54	CH3	H		441.54

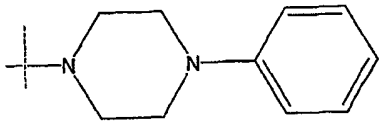
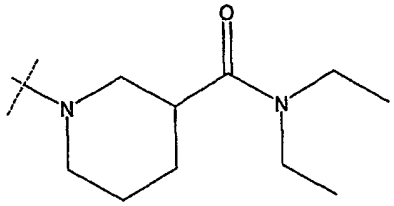
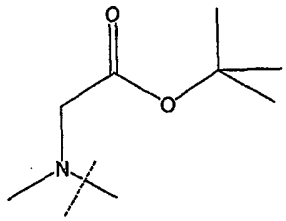
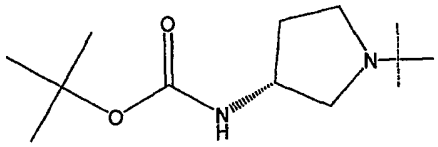
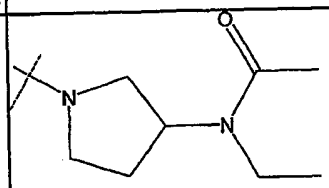
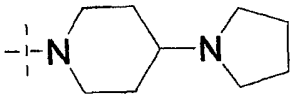
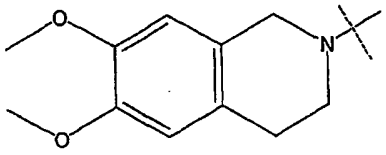
55	CH3	H		502.41
56	CH3	H		498.99
57	CH3	H		557.10
58	CH3	H		553.66
59	CH3	H		433.56

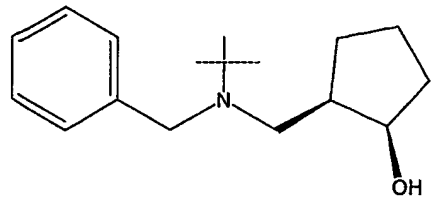
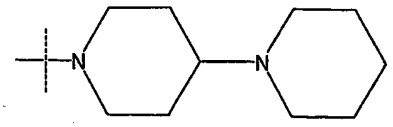
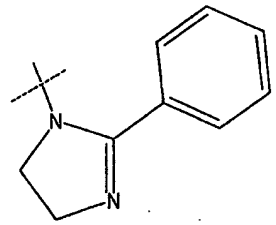
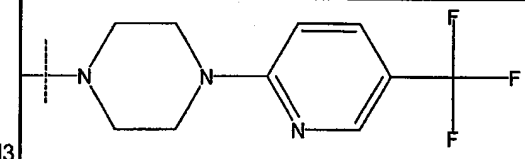
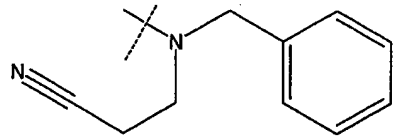
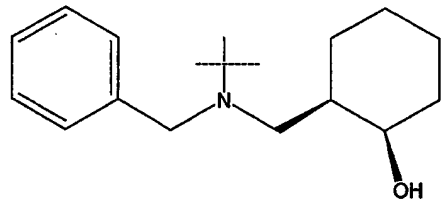
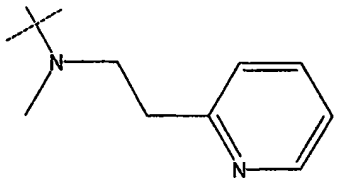
60	CH3	H		481.60
61	CH3	H		522.65
62	CH3	H		490.57
63	CH3	H		446.56
64	CH3	H		419.53

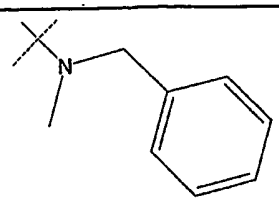
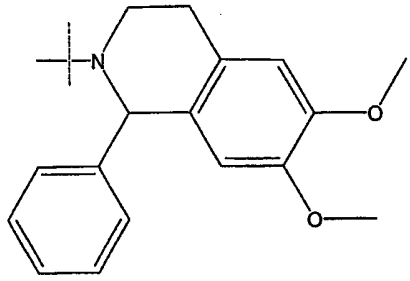
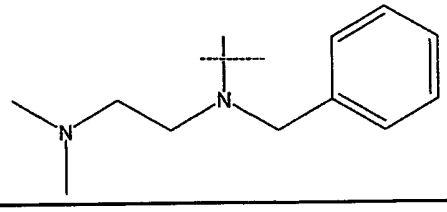
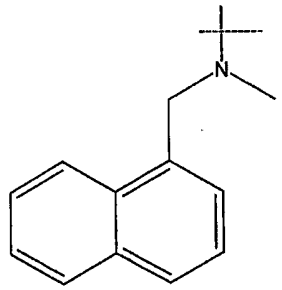
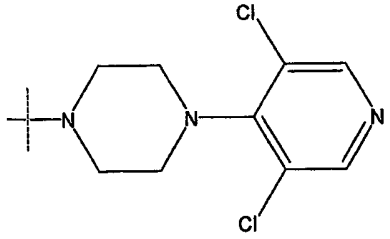
65	CH3	H		463.54
66	CH3	H		315.38
67	CH3	H		359.39
68	CH3	H		356.43
69	H	CH3		357.42
70	H	CH3		375.43
71	H	CH3		371.45
72	H	CH3		434.51

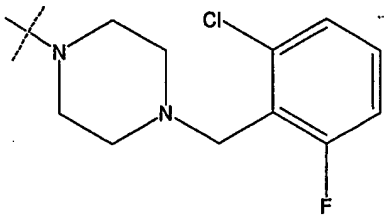
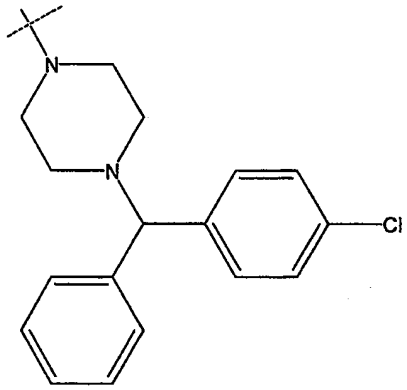
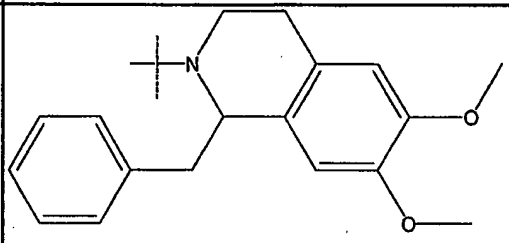
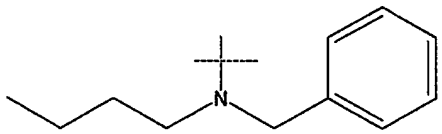
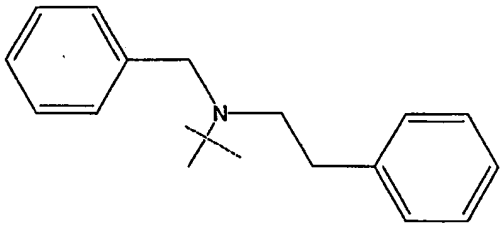
73	H	CH3		421.50
74	H	CH3		413.48
75	H	CH3		407.48
76	H	CH3		345.41
77	H	CH3		399.46
78	H	CH3		385.43

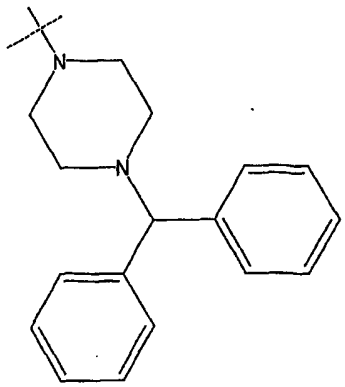
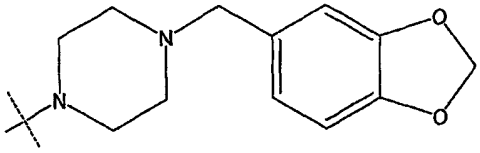
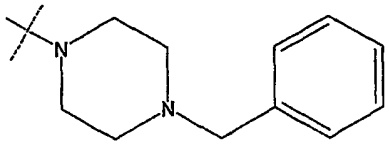
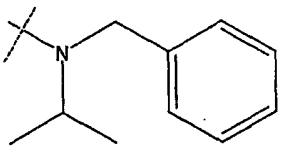
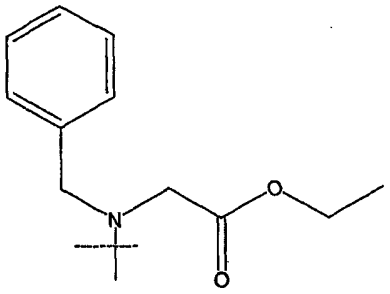
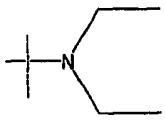
79	H	CH3		406.49
80	H	CH3		433.52
81	H	CH3		467.57
82	H	CH3		398.47
83	H	CH3		403.49
84	H	CH3		403.49
85	H	CH3		399.54
86	H	CH3		327.39

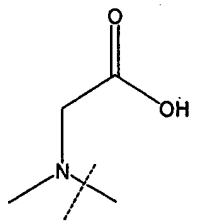
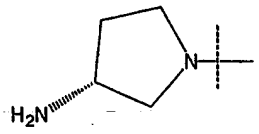
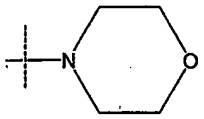
87	H	CH3		432.53
88	H	CH3		454.58
89	H	CH3		415.50
90	H	CH3		456.55
91	H	CH3		426.52
92	H	CH3		424.55
93	H	CH3		463.54

94	H	CH3		475.60
95	H	CH3		438.58
96	H	CH3		416.49
97	H	CH3		501.52
98	H	CH3		430.51
99	H	CH3		489.62
100	H	CH3		406.49

101	H	CH3		391.48
102	H	CH3		539.64
103	H	CH3		448.57
104	H	CH3		441.54
105	H	CH3		502.41

106	H	CH3		498.99
107	H	CH3		557.10
108	H	CH3		553.66
109	H	CH3		433.56
110	H	CH3		481.60

111	H	CH3		522.65
112	H	CH3		490.57
113	H	CH3		446.56
114	H	CH3		419.53
115	H	CH3		463.54
116	H	CH3		343.44

117	H	CH3		359.39
118	H	CH3		356.43
119	H	H		343.39

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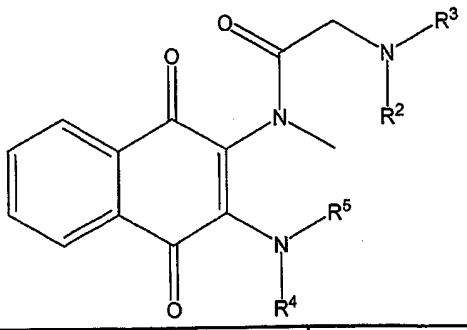
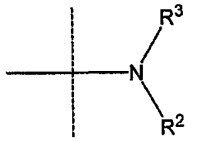
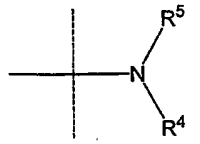
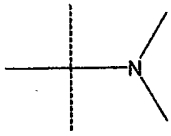
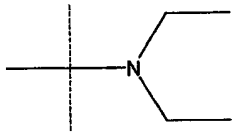
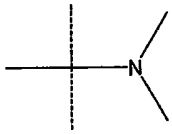
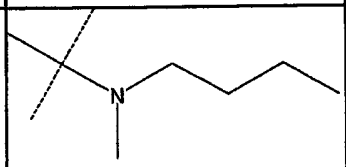
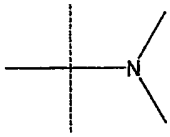
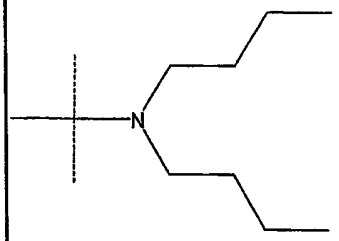
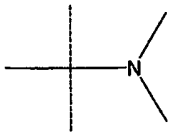
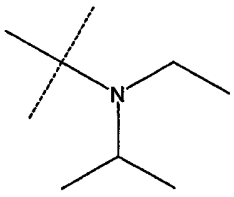
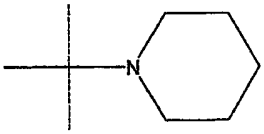
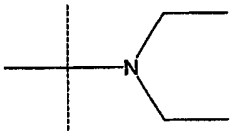
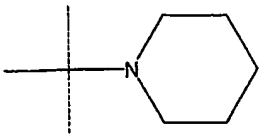
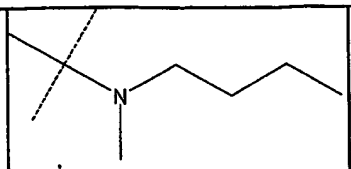
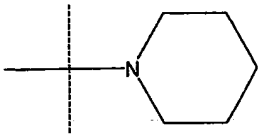
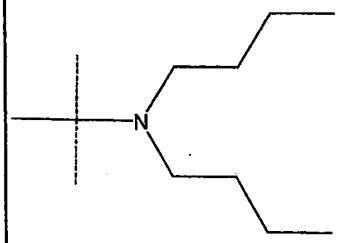
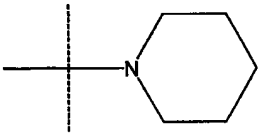
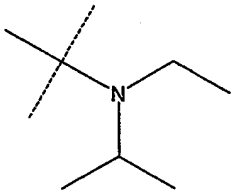
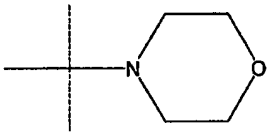
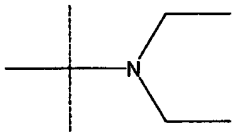
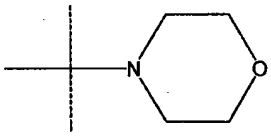
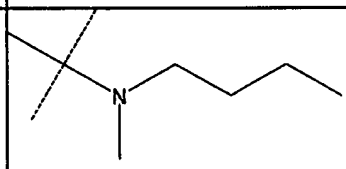
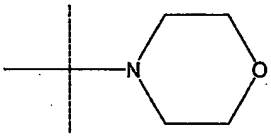
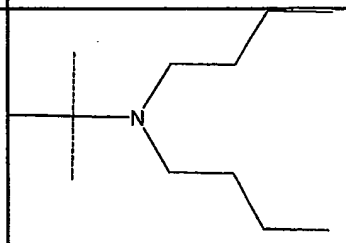
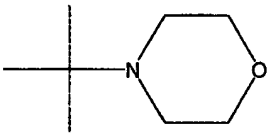
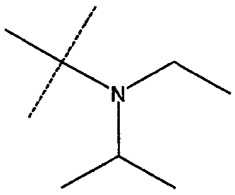
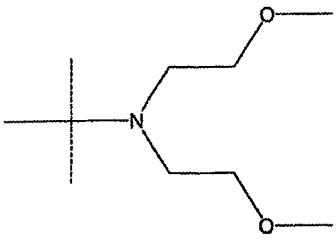
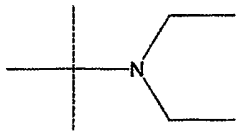
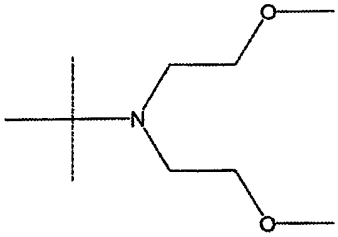
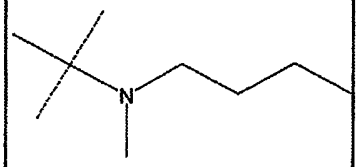
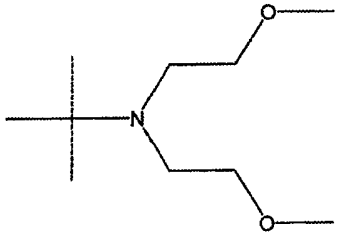
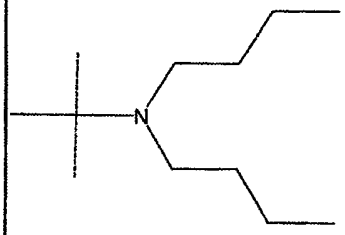
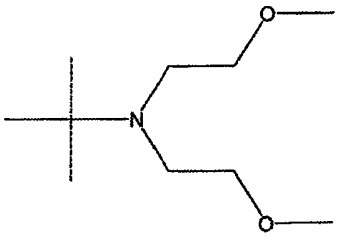
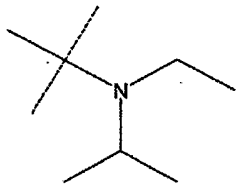
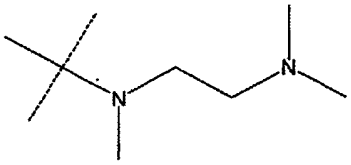
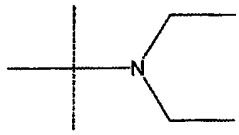
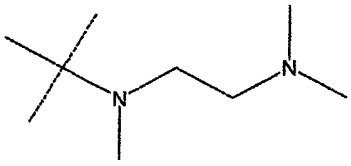
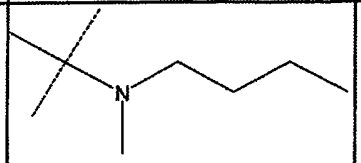
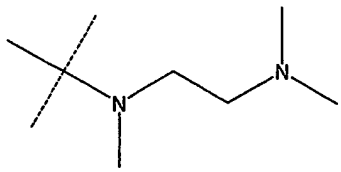
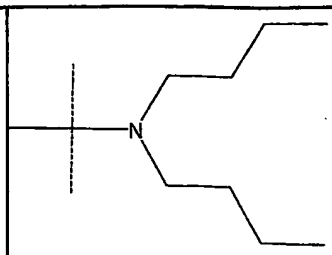
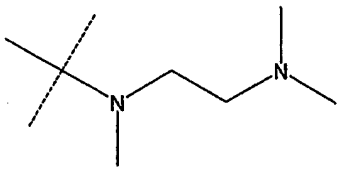
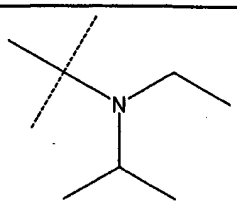
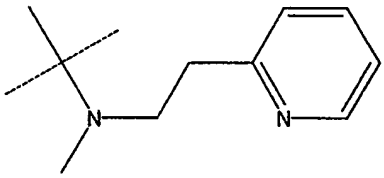
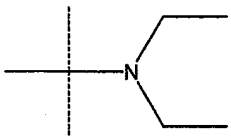
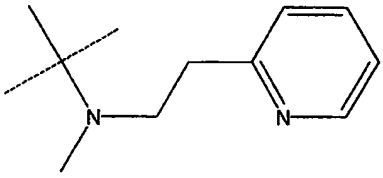
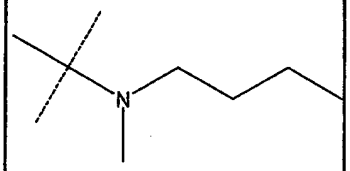
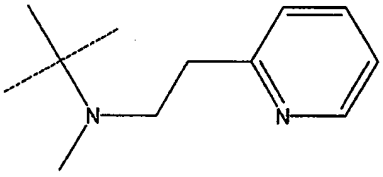
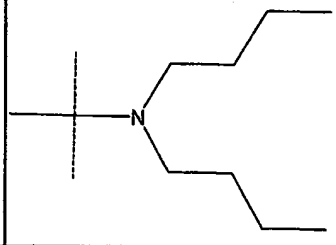
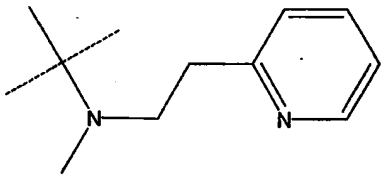
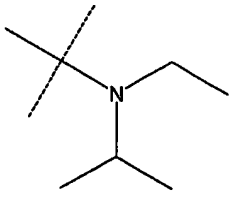


Cmpd			MW
1			343.42
2			357.45
3			399.53
4			357.45
5			383.48

6			397.51
7			439.59
8			397.51
9			385.46
10			399.48
11			441.56
12			399.48

13			431.53
14			445.55
15			487.63
16			445.55
17			400.51
18			414.54

19			456.62
20			414.54
21			434.53
22			448.56
23			490.64
24			448.56

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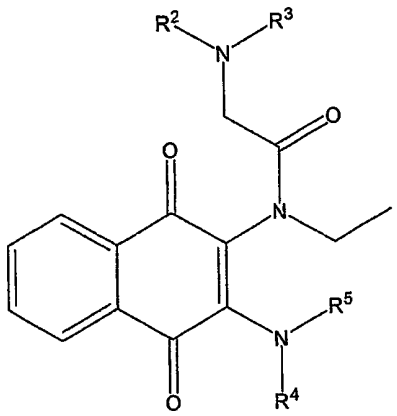
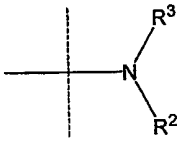
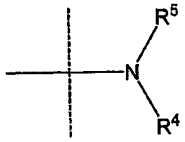
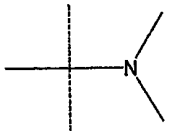
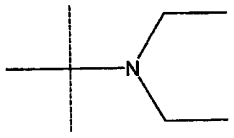
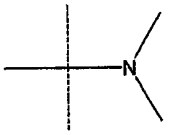
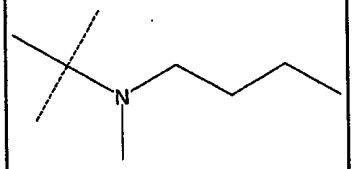
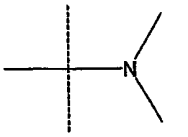
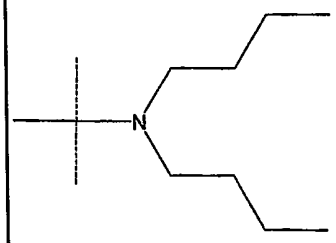
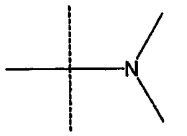
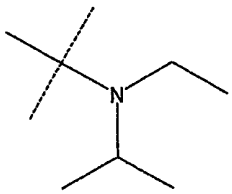
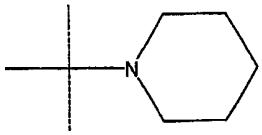
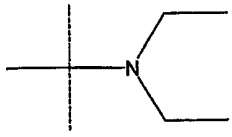
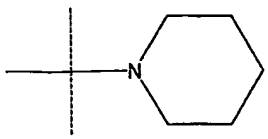
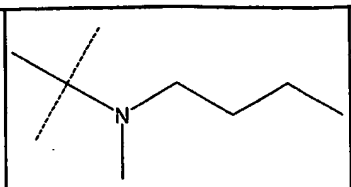
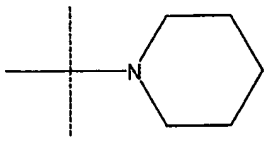
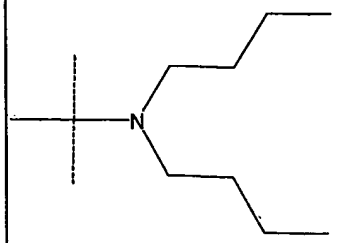
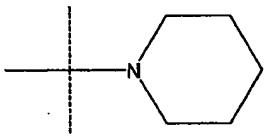
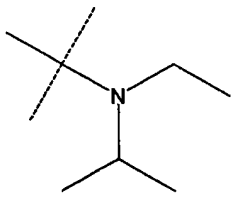
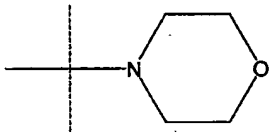
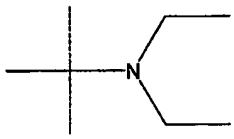
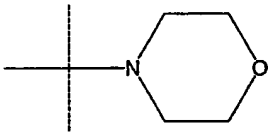
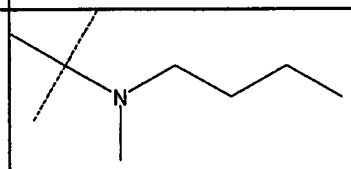
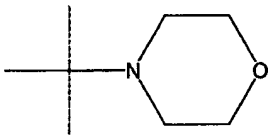
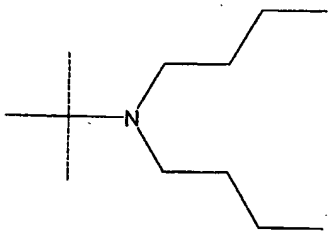
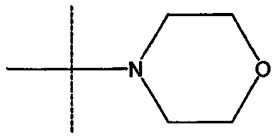
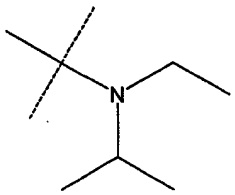
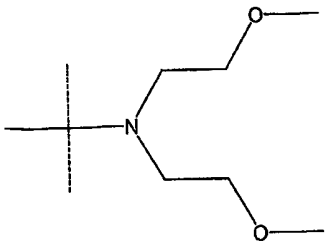
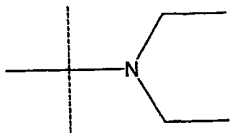
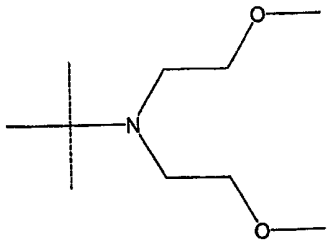
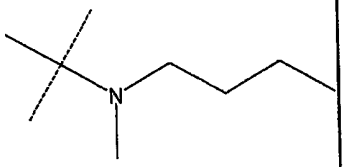
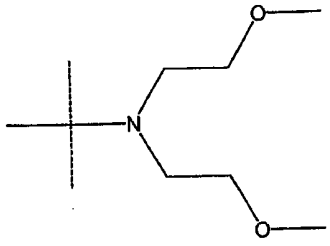
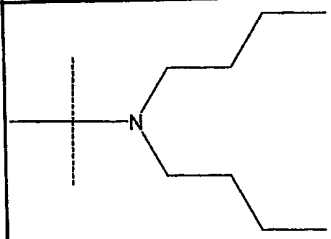
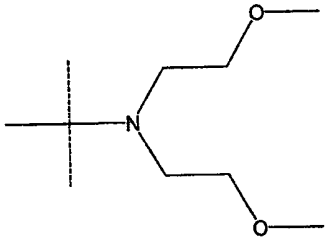
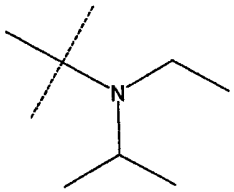
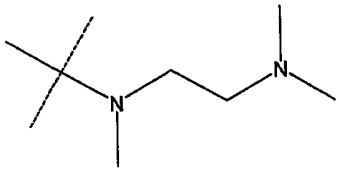
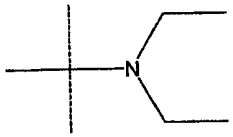
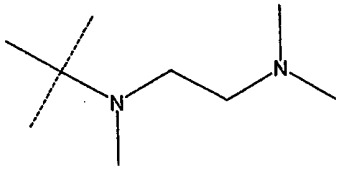
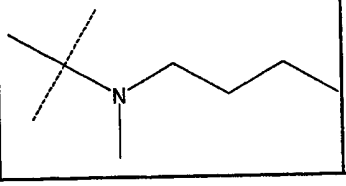
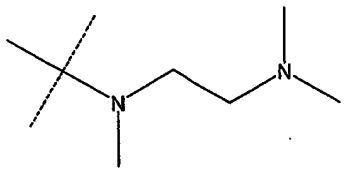
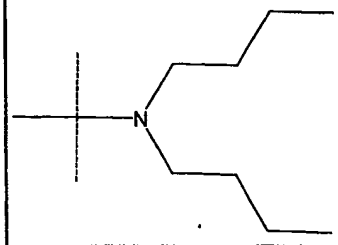
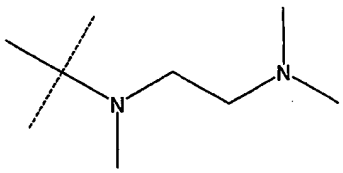
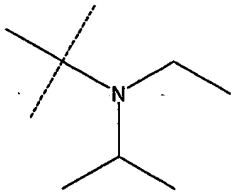
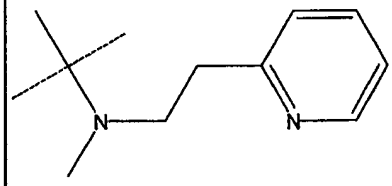
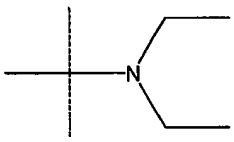
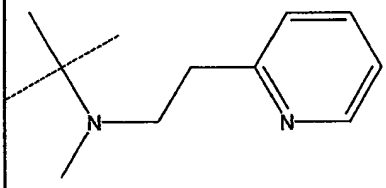
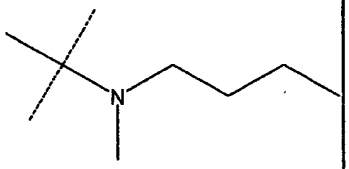
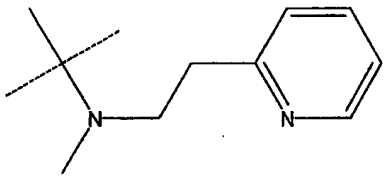
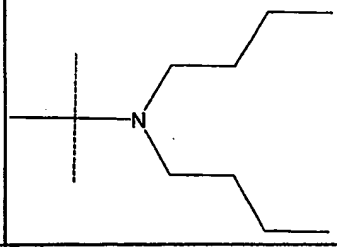
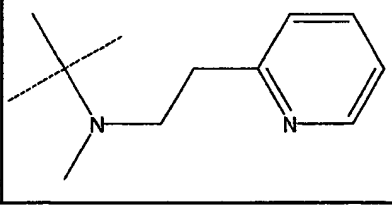
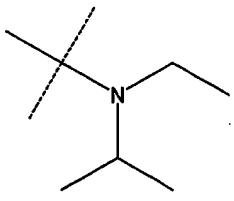


Cmpd			MW
1			357.45
2			371.47
3			413.55
4			371.47
5			397.51

6			411.54
7			453.62
8			411.54
9			399.48
10			413.51
11			455.59
12			413.51

13			445.55
14			459.58
15			501.66
16			443.58
17			414.54
18			428.57

19			470.65
20			428.57
21			448.56
22			462.58
23			504.66
24			462.58

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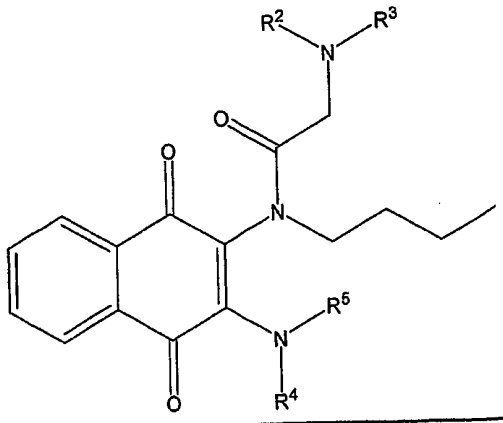
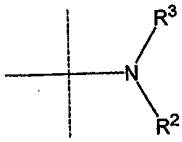
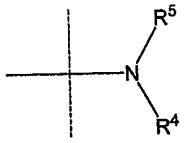
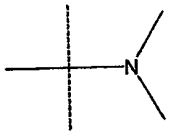
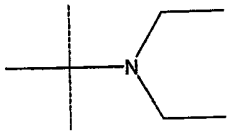
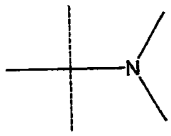
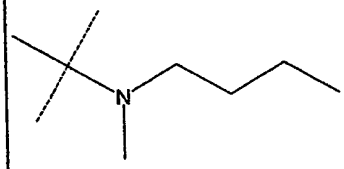
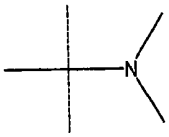
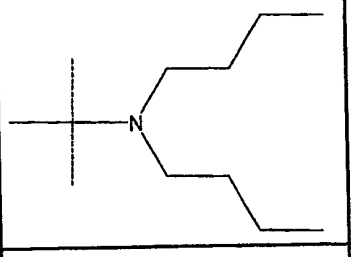
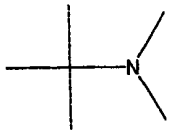
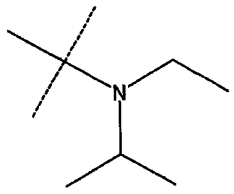
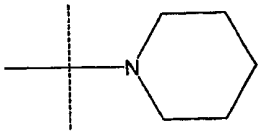
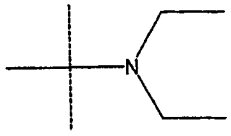
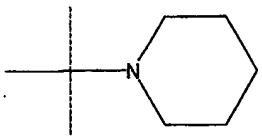
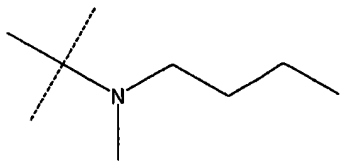
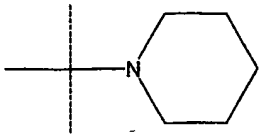
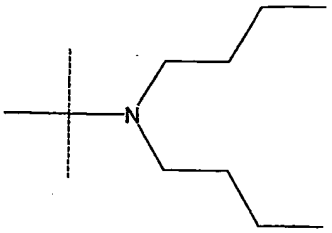
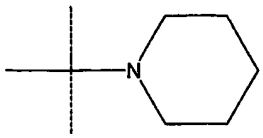
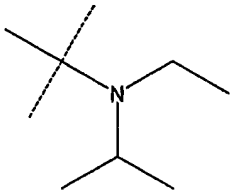
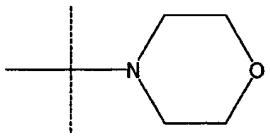
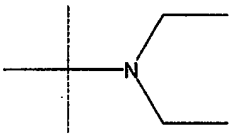
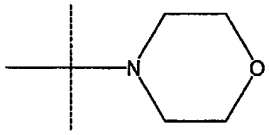
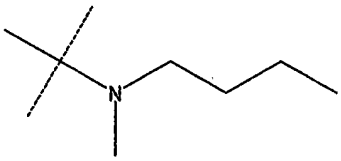
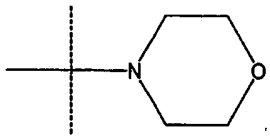
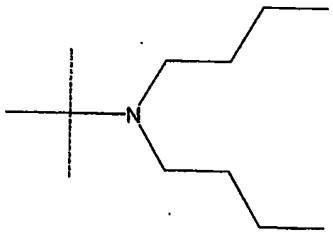
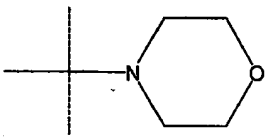
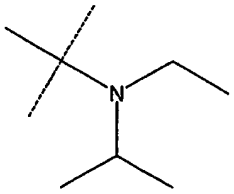
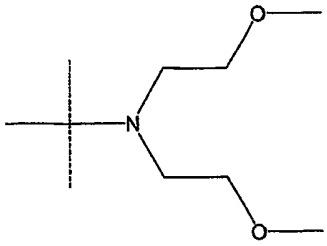
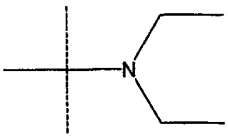
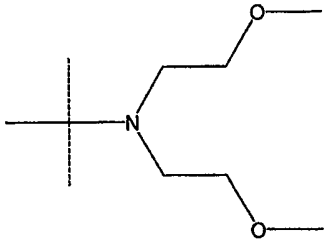
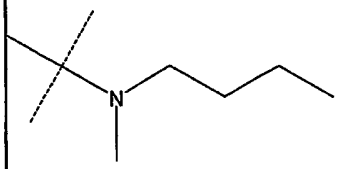
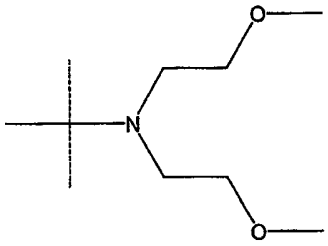
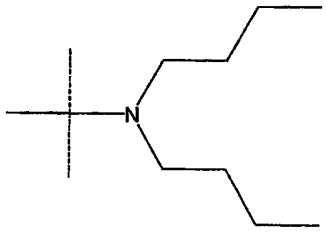
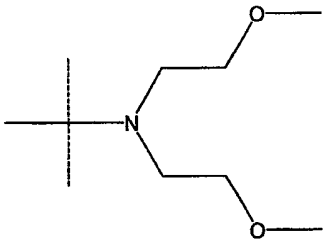
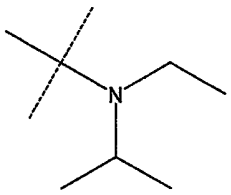
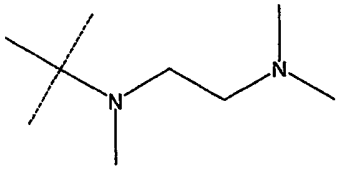
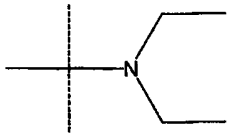
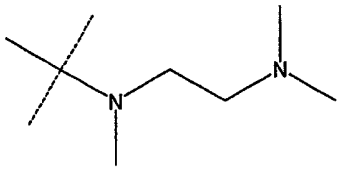
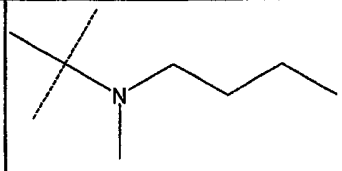
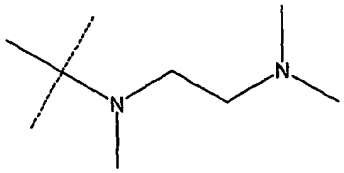
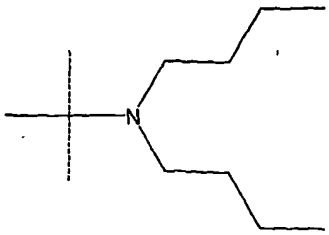
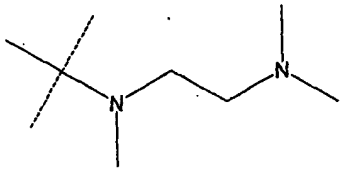
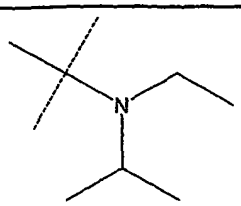
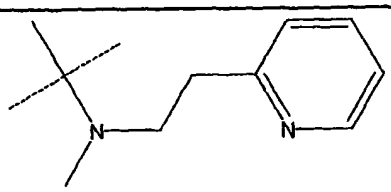
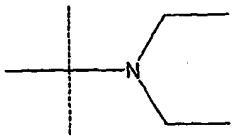
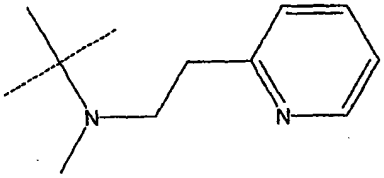
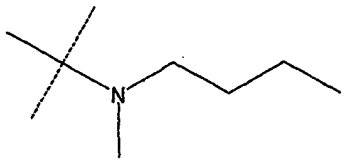
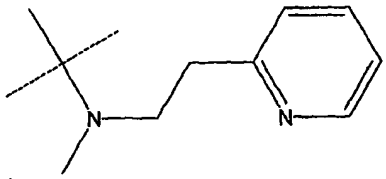
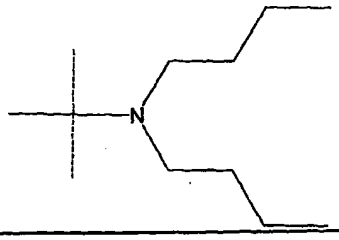
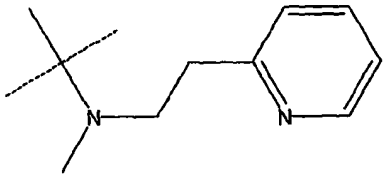
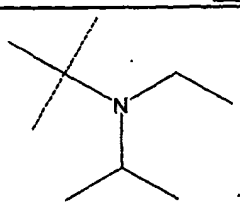


Cpmd			MW
1			385.50
2			399.53
3			441.61
4			399.53
5			425.56

6			439.59
7			481.67
8			439.59
9			427.54
10			441.56
11			483.64
12			441.56

13			473.6
14			487.63
15			529.71
16			487.63
17			442.59
18			456.62

19			498.7
20			456.62
21			476.61
22			490.64
23			532.72
24			490.64

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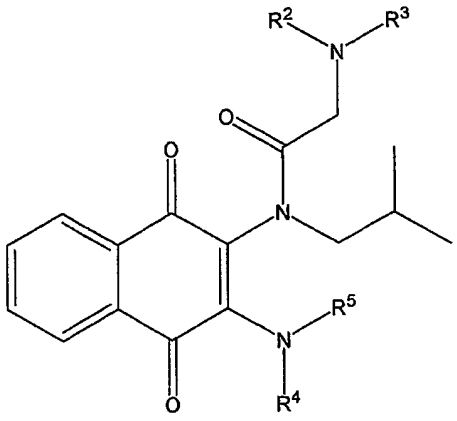
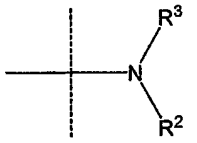
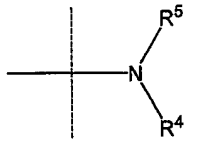
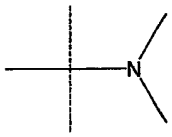
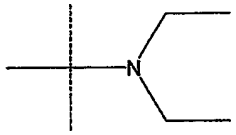
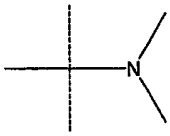
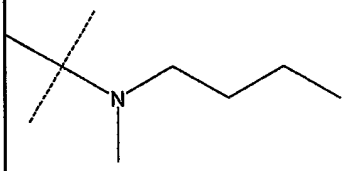
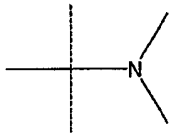
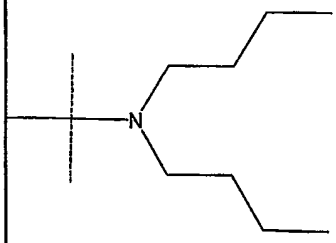
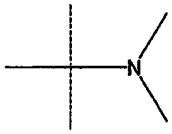
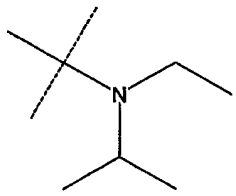
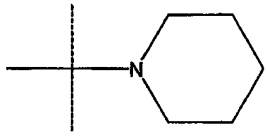
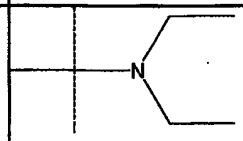
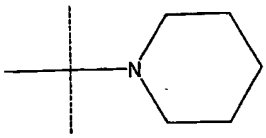
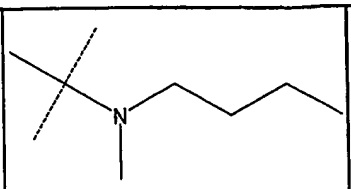
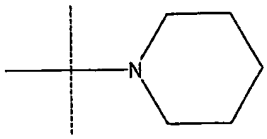
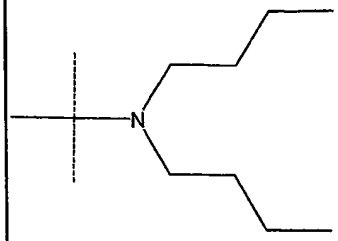
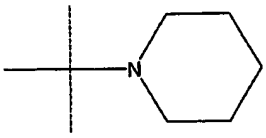
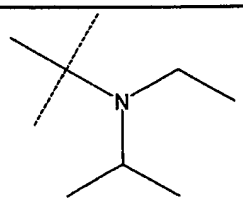
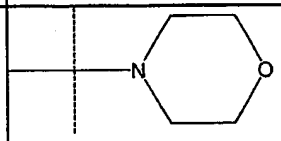
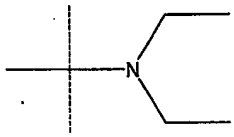
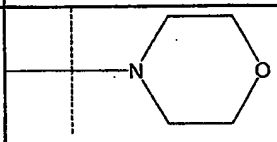
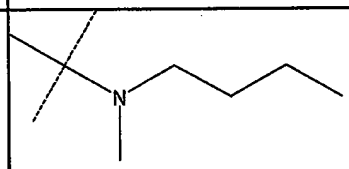
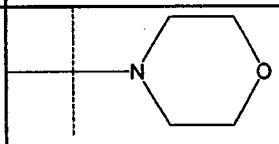
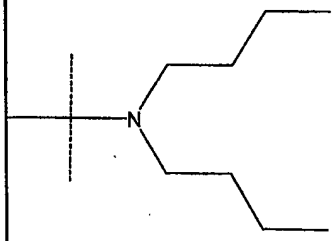
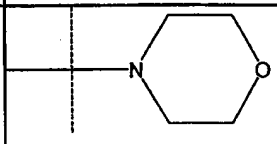
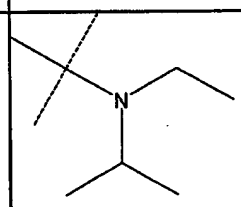
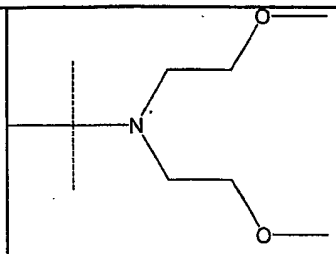
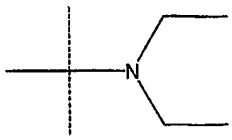
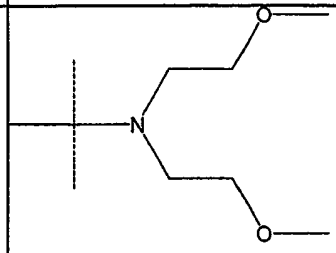
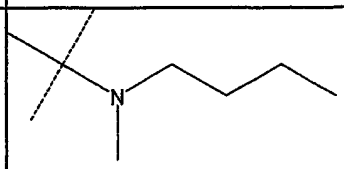
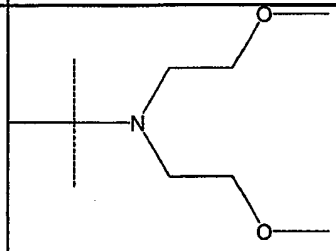
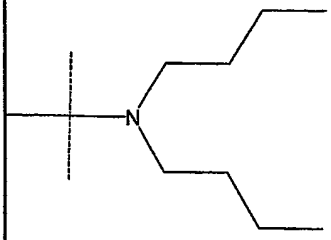
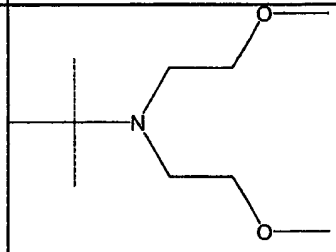
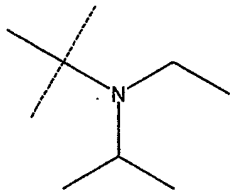
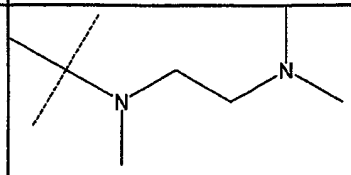
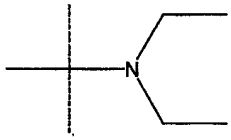
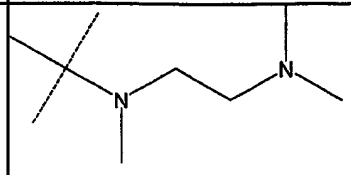
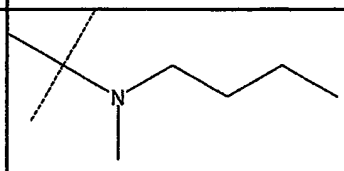


Cmpd			MW
1			385.50
2			399.53
3			441.61
4			399.53
5			425.56

6			439.59
7			481.67
8			439.59
9			427.54
10			441.56
11			483.64
12			441.56

13			473.6
14			487.63
15			529.71
16			487.63
17			442.59
18			456.62

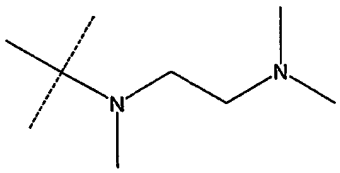
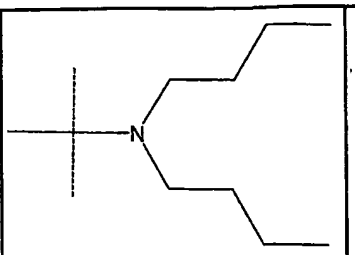
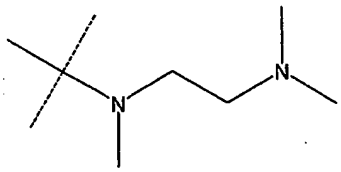
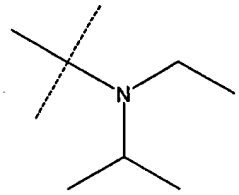
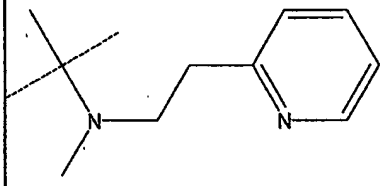
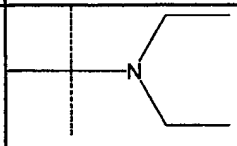
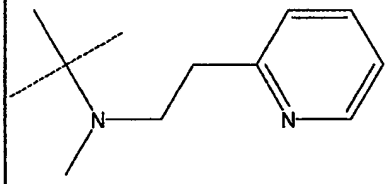
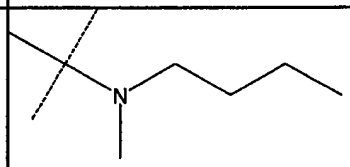
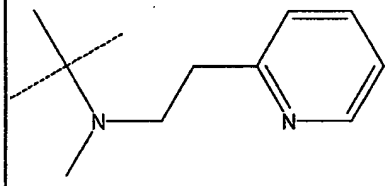
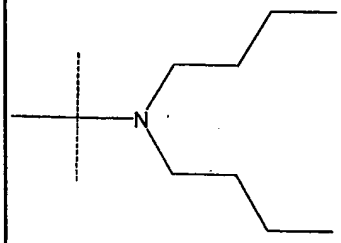
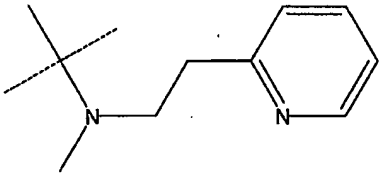
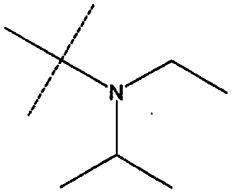
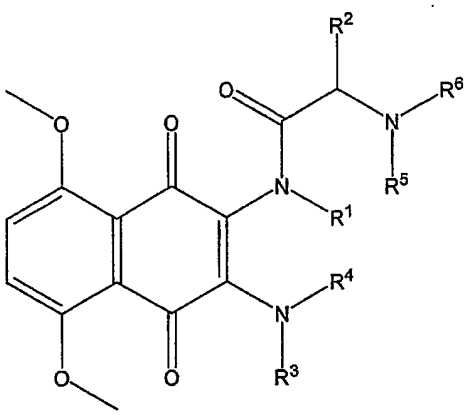
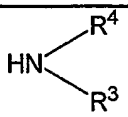
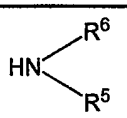
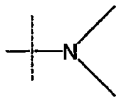
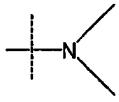
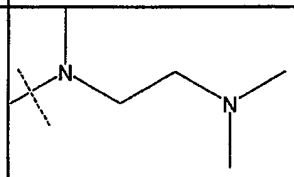
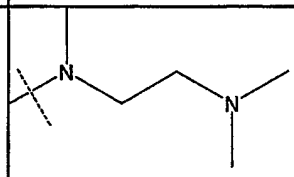
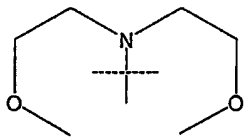
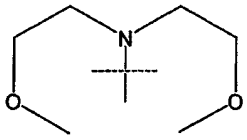
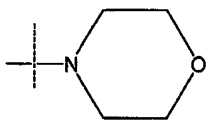
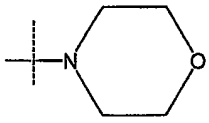
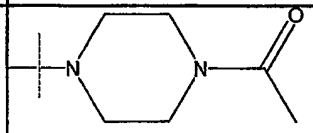
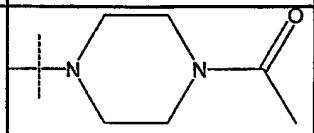
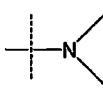
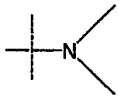
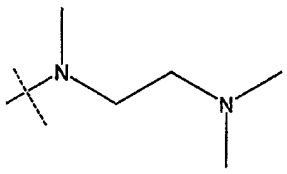
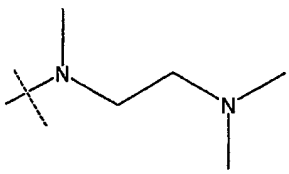
19			498.7
20			456.62
21			476.61
22			490.64
23			532.72
24			490.64

Table 7



Cmpd	R_1	R_2			MW
1	CH3	H			375.42
2	CH3	H			489.61
3	CH3	H			551.63
4	CH3	H			459.49
5	CH3	H			541.60
6	H	CH3			375.42
7	H	CH3			489.61

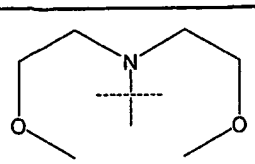
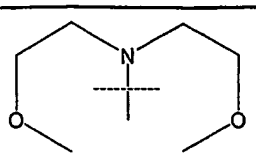
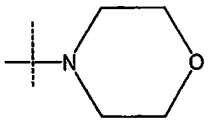
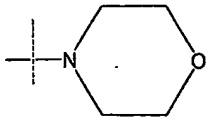
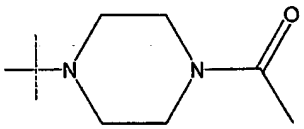
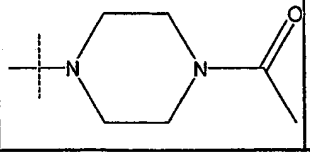
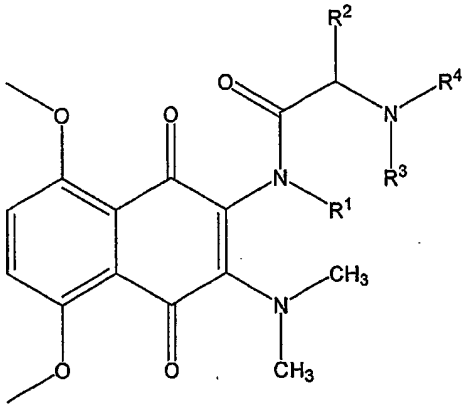
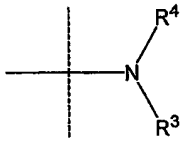
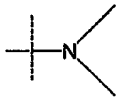
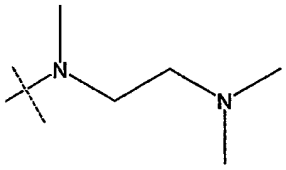
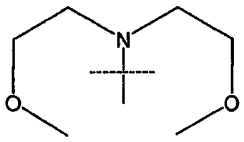
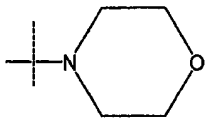
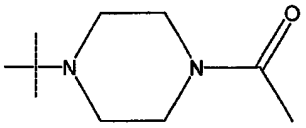
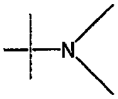
8	H	CH3			551.63
9	H	CH3			459.49
10	H	CH3			541.60

Table 8



Cmpd	R_1	R_2		MW
1	CH3	H		375.42
2	CH3	H		432.51
3	CH3	H		463.52
4	CH3	H		417.45
5	CH3	H		458.51
6	H	CH3		375.42

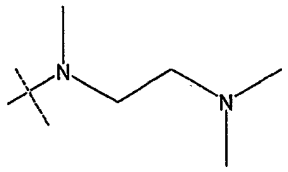
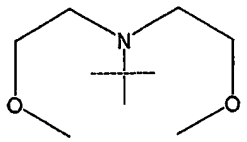
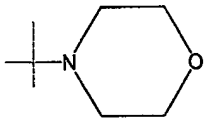
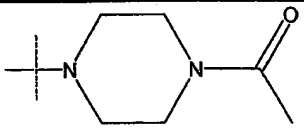
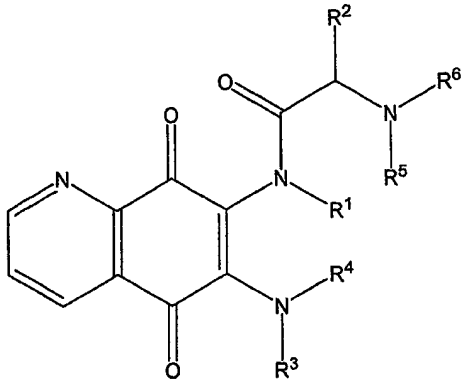
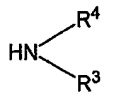
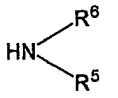
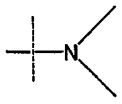
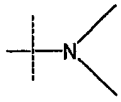
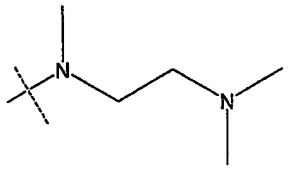
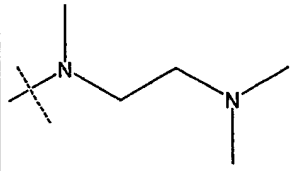
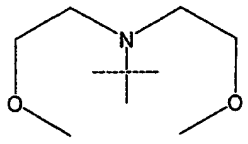
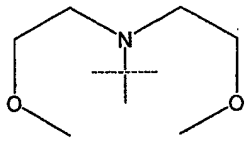
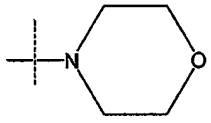
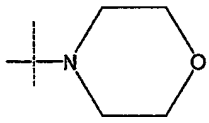
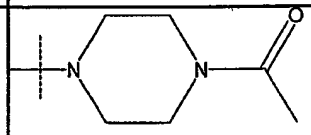
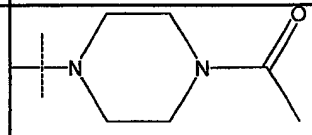
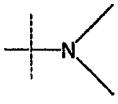
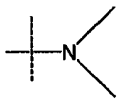
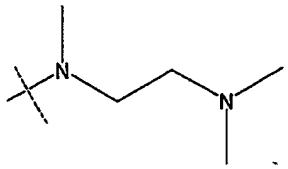
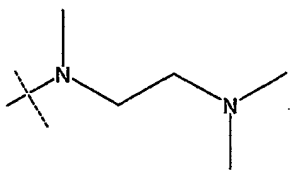
7	H	CH3		432.51
8	H	CH3		463.52
9	H	CH3		417.45
10	H	CH3		458.51

Table 9



Cmpd	R_1	R_2			MW
1	CH3	H			316.35
2	CH3	H			430.54
3	CH3	H			492.57
4	CH3	H			400.43
5	CH3	H			482.53
6	H	CH3			316.35
7	H	CH3			430.54

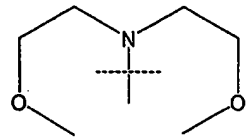
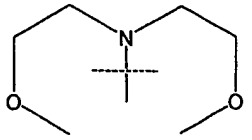
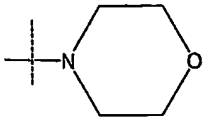
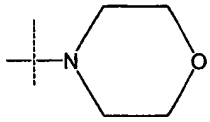
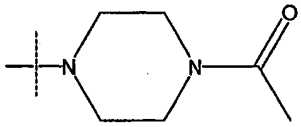
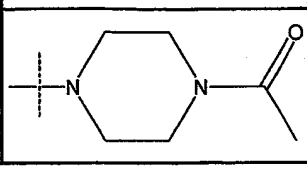
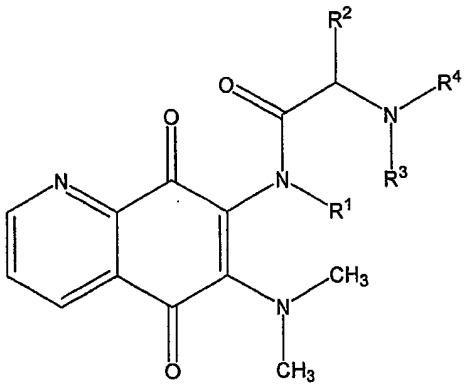
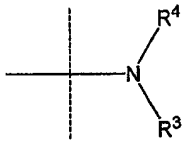
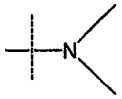
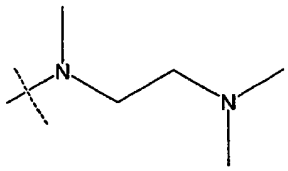
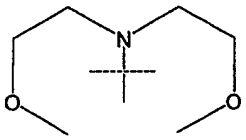
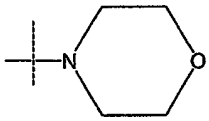
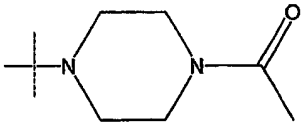
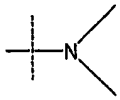
8	H	CH3			492.57
9	H	CH3			400.43
10	H	CH3			482.53

Table 10



Cmpd	R_1	R_2		MW
1	CH3	H		316.35
2	CH3	H		373.45
3	CH3	H		404.46
4	CH3	H		358.39
5	CH3	H		399.44
6	H	CH3		316.35

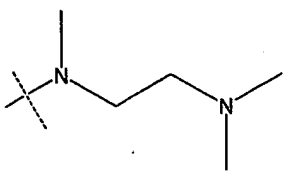
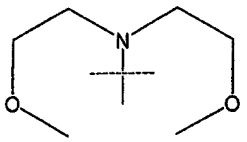
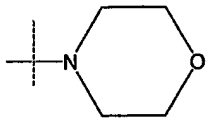
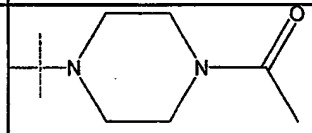
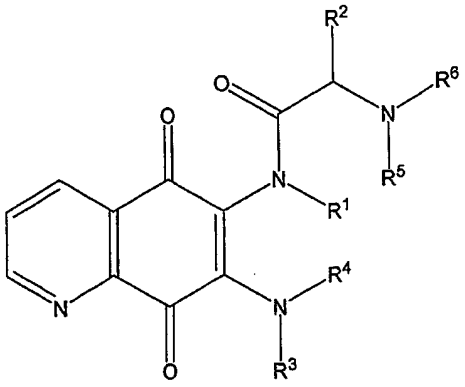
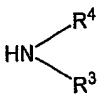
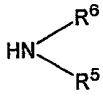
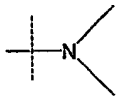
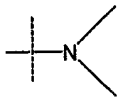
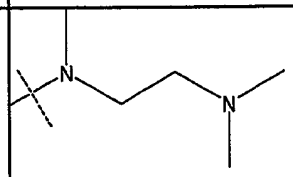
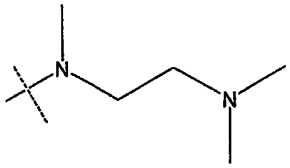
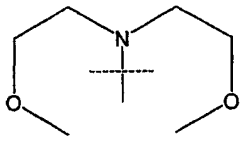
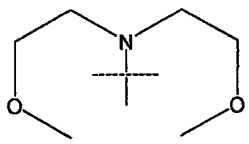
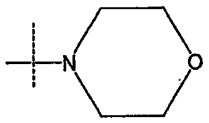
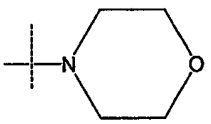
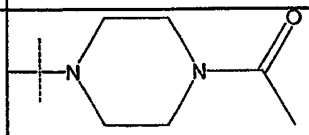
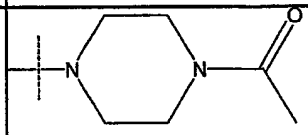
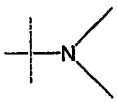
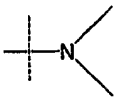
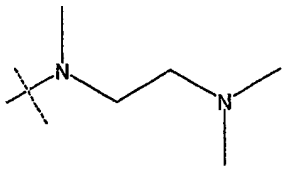
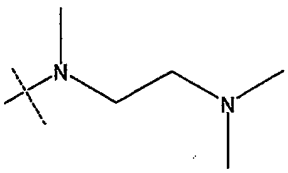
7	H	CH3		373.45
8	H	CH3		404.46
9	H	CH3		358.39
10	H	CH3		399.44

Table 11



Cmpd	R_1	R_2			MW
1	CH3	H			316.35
2	CH3	H			430.54
3	CH3	H			492.57
4	CH3	H			400.43
5	CH3	H			482.53
6	H	CH3			316.35
7	H	CH3			430.54

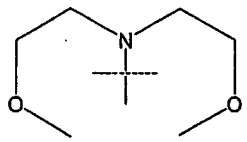
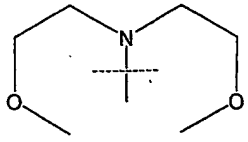
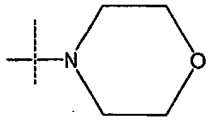
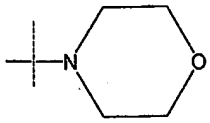
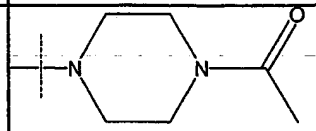
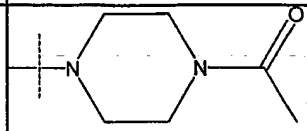
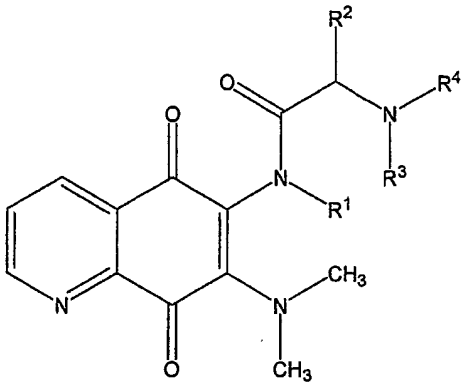
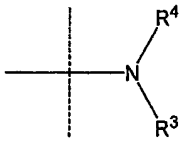
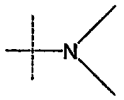
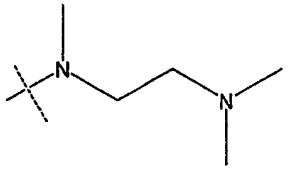
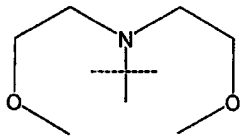
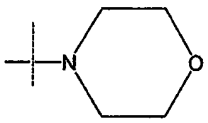
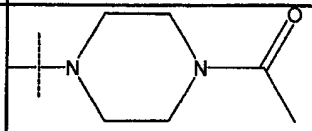
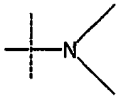
8	H	CH3			492.57
9	H	CH3			400.43
10	H	CH3			482.53

Table 12



Cmpd	R_1	R_2		MW
1	CH3	H		316.35
2	CH3	H		373.45
3	CH3	H		404.46
4	CH3	H		358.39
5	CH3	H		399.44
6	H	CH3		316.35

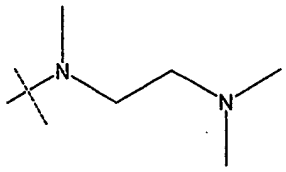
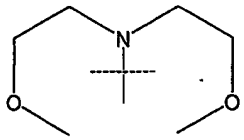
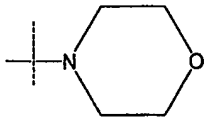
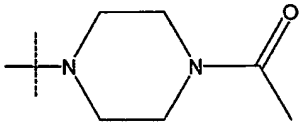
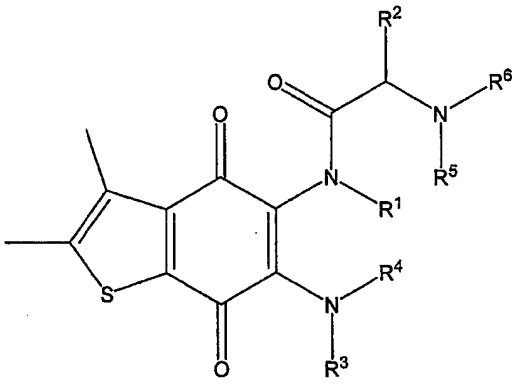
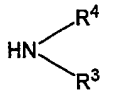
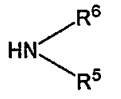
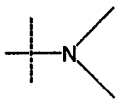
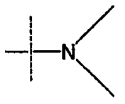
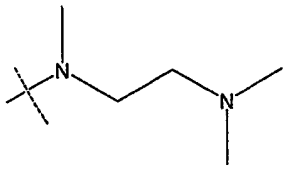
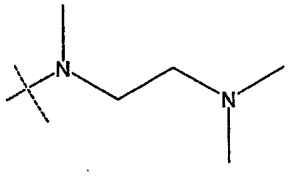
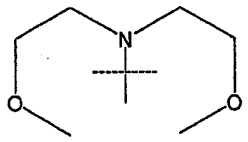
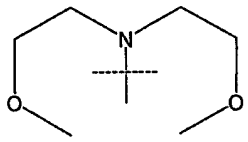
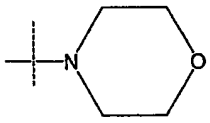
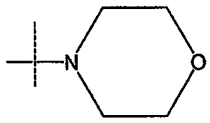
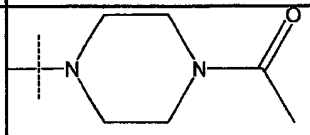
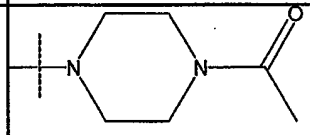
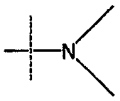
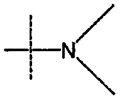
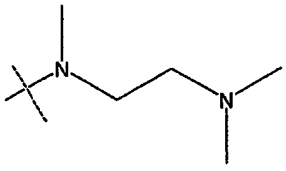
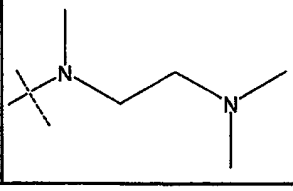
7	H	CH3		373.45
8	H	CH3		404.46
9	H	CH3		358.39
10	H	CH3		399.44

Table 13



Cmpd	R_1	R_2			MW
1	CH3	H			349.45
2	CH3	H			463.64
3	CH3	H			525.66
4	CH3	H			433.52
5	CH3	H			515.63
6	H	CH3			349.45
7	H	CH3			463.64

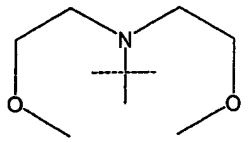
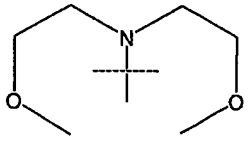
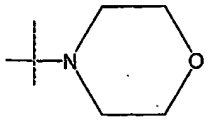
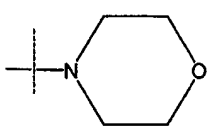
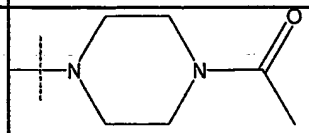
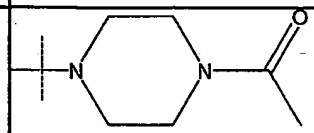
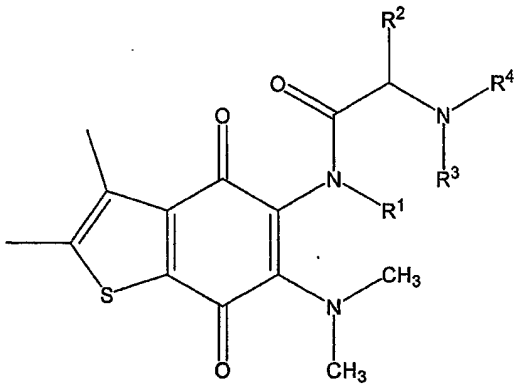
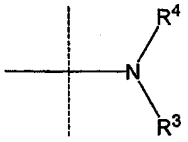
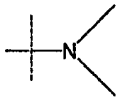
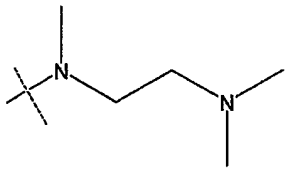
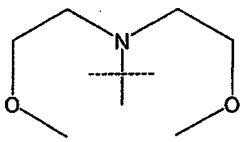
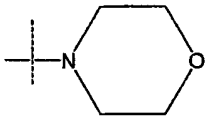
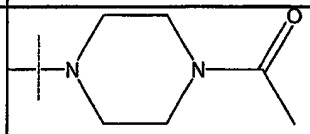
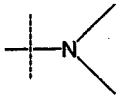
8	H	CH3			525.66
9	H	CH3			433.52
10	H	CH3			515.63

Table 14



Cmpd	R_1	R_2		MW
1	CH3	H		349.45
2	CH3	H		406.54
3	CH3	H		437.55
4	CH3	H		391.48
5	CH3	H		432.54
6	H	CH3		349.45

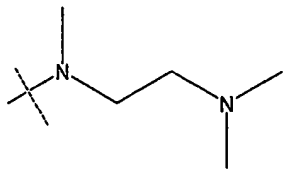
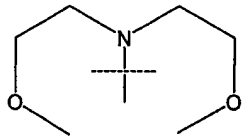
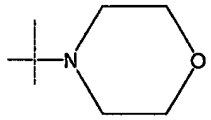
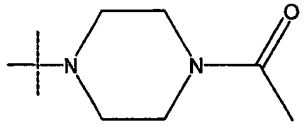
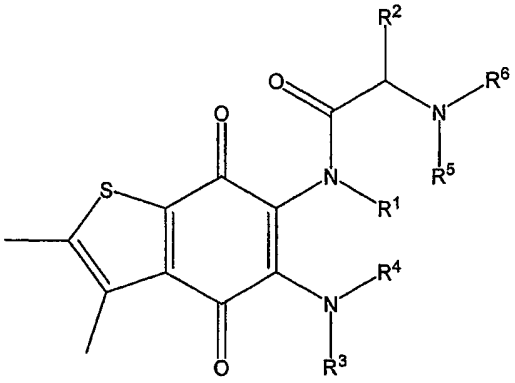
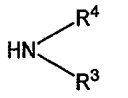
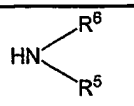
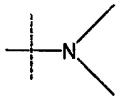
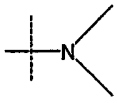
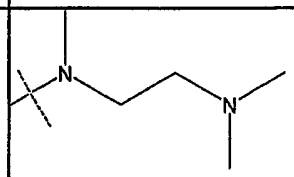
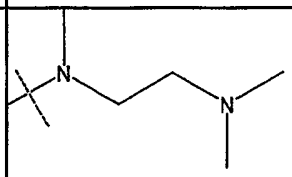
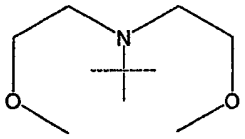
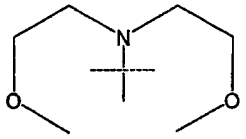
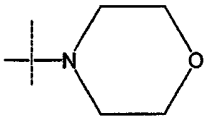
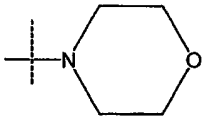
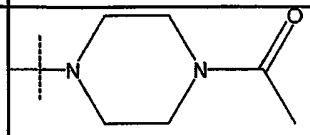
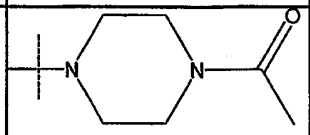
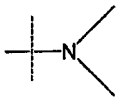
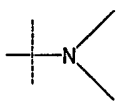
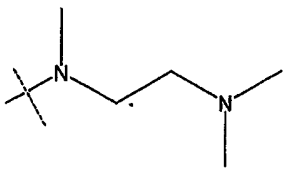
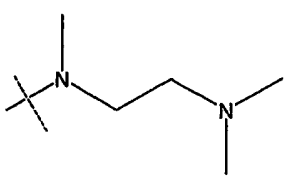
7	H	CH3		406.54
8	H	CH3		437.55
9	H	CH3		391.48
10	H	CH3		432.54

Table 15



Cmpd	R_1	R_2			MW
1	CH3	H			349.45
2	CH3	H			463.64
3	CH3	H			525.66
4	CH3	H			433.52
5	CH3	H			515.63
6	H	CH3			349.45
7	H	CH3			463.64

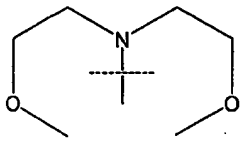
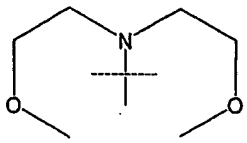
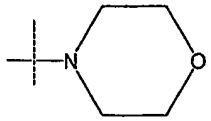
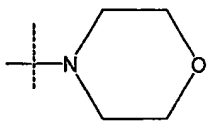
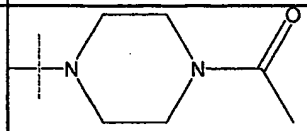
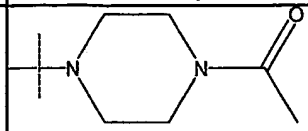
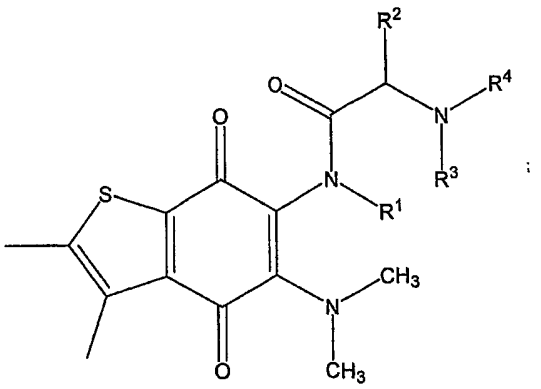
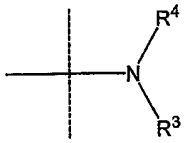
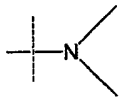
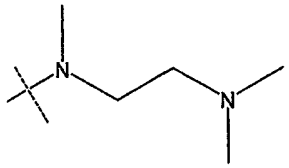
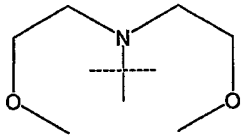
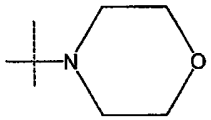
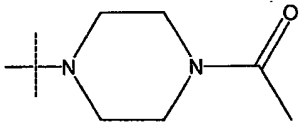
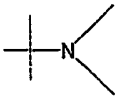
8	H	CH3			525.66
9	H	CH3			433.52
10	H	CH3			515.63

Table 16



Cmpd	R_1	R_2		MW
1	CH3	H		349.45
2	CH3	H		406.54
3	CH3	H		437.55
4	CH3	H		391.48
5	CH3	H		432.54
6	H	CH3		349.45

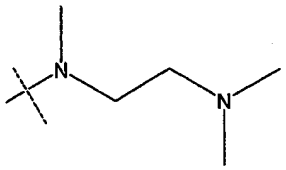
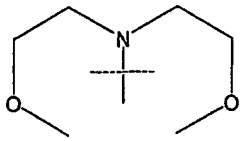
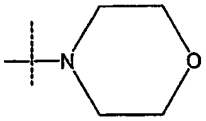
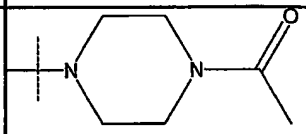
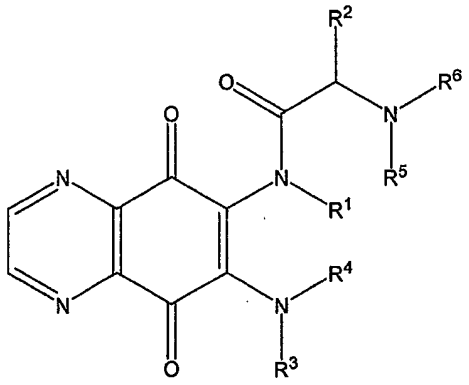
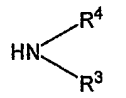
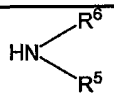
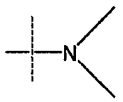
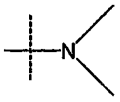
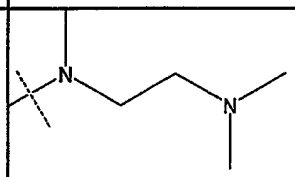
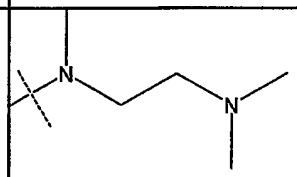
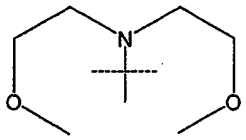
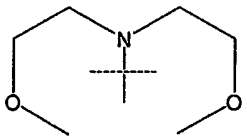
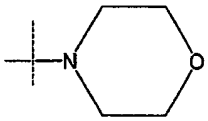
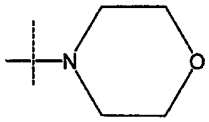
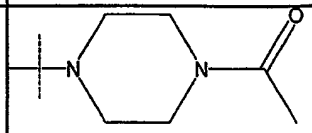
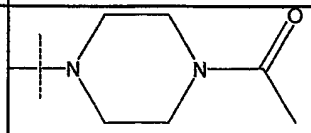
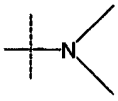
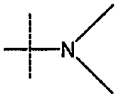
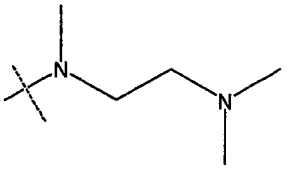
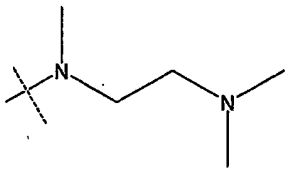
7	H	CH3		406.54
8	H	CH3		437.55
9	H	CH3		391.48
10	H	CH3		432.54

Table 17



Cmpd	R_1	R_2			MW
1	CH3	H			317.34
2	CH3	H			431.53
3	CH3	H			493.55
4	CH3	H			401.42
5	CH3	H			483.52
6	H	CH3			317.34
7	H	CH3			431.53

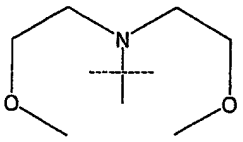
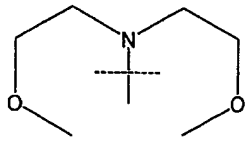
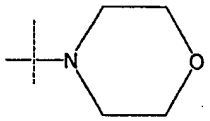
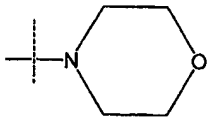
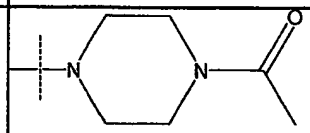
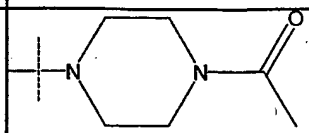
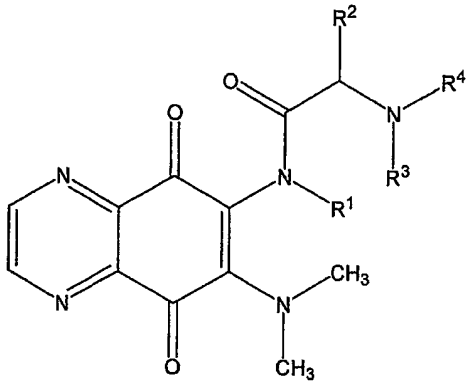
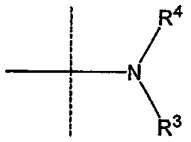
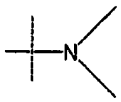
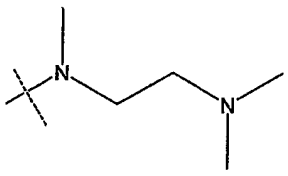
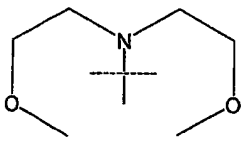
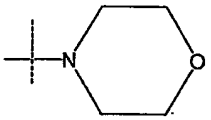
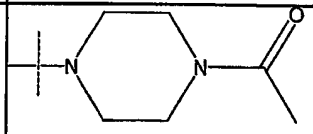
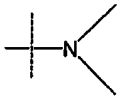
8	H	CH3			493.55
9	H	CH3			401.42
10	H	CH3			483.52

Table 18



Cmpd	R_1	R_2		MW
1	CH3	H		317.34
2	CH3	H		374.44
3	CH3	H		405.45
4	CH3	H		359.38
5	CH3	H		400.43
6	H	CH3		317.34

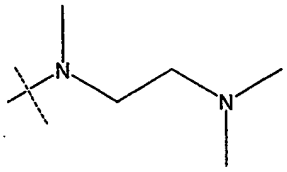
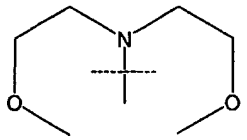
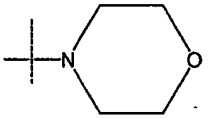
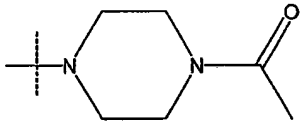
7	H	CH3		374.44
8	H	CH3		405.45
9	H	CH3		359.38
10	H	CH3		400.43

Table 19

Gene No.	Gene Identifier	Gene Name
1	XM_011929	RTP801
2	NM_004864	prostate differentiation factor
3	NM_001657	amphiregulin (schwannoma-derived growth factor)
4	XM_033762	GRB10
5	NM_004083	DNA-damage-inducible transcript 3
6	XM_009097	PPP1R15A
7	NM_005542	insulin induced gene 1
8	XM_032884	MGC11324
9	XM_052673	VEGF
10	NM_007235	exportin, tRNA (nuclear export receptor for tRNAs)
11	NM_000179	mutS homolog 6 (E. coli)
12	NM_005194	CCAAT/enhancer binding protein (C/EBP), beta
13	XM_043412	CDKN1A
14	NM_004448	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma de
15	NM_004526	MCM2 minichromosome maintenance deficient 2, mitotin (S. cerevisiae)
16	XM_035627	UHRF1
17	L24498	GADD45A
18	NM_005915	MCM6 minichromosome maintenance deficient 6 (MIS5 homolog, S. pombe) (S. cerevis
19	NM_004642	CDK2-associated protein 1
20	NM_004629	Fanconi anemia, complementation group G
21	NM_022119	protease, serine, 22
22	XM_002003	STMN1
23	NM_014736	KIAA0101 gene product
24	NM_002691	polymerase (DNA directed), delta 1, catalytic subunit 125kDa
25	XM_034901	MSH2
26	XM_001284	MDM4
27	XM_018276	FLJ13782
28	NM_004707	APG12 autophagy 12-like (S. cerevisiae)
29	NM_004836	eukaryotic translation initiation factor 2-alpha kinase 3
30	XM_008618	CBX4
31	NM_003504	CDC45 cell division cycle 45-like (S. cerevisiae)
32	XM_002242	HAT1
33	NM_014331	solute carrier family 7, (cationic amino acid transporter, y+ system) member 11
34	NM_003467	chemokine (C-X-C motif) receptor 4
35	XM_002899	CDC25A
36	NM_006349	putative cyclin G1 interacting protein
37	XM_056035	PCNA
38	XM_003511	EREG
39	XM_031515	RAD51
40	XM_017925	EIF4E
41	NM_001799	cyclin-dependent kinase 7 (MO15 homolog, Xenopus laevis, cdk-activating kinase)
42	NM_004990	methionine-tRNA synthetase
43	NM_057749	cyclin E2
44	NM_001540	heat shock 27kDa protein 1

45	NM_005882	macrophage erythroblast attacher
46	XM_047059	SUV39H1
47	NM_006156	neural precursor cell expressed, developmentally down-regulated 8
48	NM_016395	butyrate-induced transcript 1
49	XM_012472	NPIP
50	NM_018518	MCM10 minichromosome maintenance deficient 10 (S. cerevisiae)
51	NM_000194	hypoxanthine phosphoribosyltransferase 1 (Lesch-Nyhan syndrome)
52	NM_002359	v-maf musculoaponeurotic fibrosarcoma oncogene homolog G (avian)
53	XM_001589	DVL1
54	NM_003276	thymopoietin
55	XM_040103	DLC1
56	XM_010272	RBBP7
57	NM_001226	caspase 6, apoptosis-related cysteine protease
58	NM_013376	CDK4-binding protein p34SEI1
59	NM_001196	BH3 interacting domain death agonist
60	AF317391	BCL-6 interacting corepressor
61	NM_002435	mannose phosphate isomerase
62	NM_003503	CDC7 cell division cycle 7-like 1 (S. cerevisiae)
63	NM_001168	baculoviral IAP repeat-containing 5 (survivin)
64	XM_036462	ACLY
65	XM_009643	RBL1
66	NM_001424	epithelial membrane protein 2
67	AK057120	high-mobility group box 1
68	XM_051677	CDKN3
69	NM_001379	DNA (cytosine-5-)-methyltransferase 1
70	XM_001668	PDZK1
71	NM_001967	eukaryotic translation initiation factor 4A, isoform 2
72	XM_050297	XRCC3
73	NM_004428	ephrin-A1
74	AB037790	heme-regulated initiation factor 2-alpha kinase
75	NM_007306	breast cancer 1, early onset
76	NM_004336	BUB1 budding uninhibited by benzimidazoles 1 homolog (yeast)
77	NM_031844	heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A)
78	XM_002943	POLQ
79	D21262	nucleolar and coiled-body phosphoprotein 1
80	XM_056165	YWHAH
81	NM_006609	mitogen-activated protein kinase kinase kinase 2
82	NM_013258	apoptosis-associated speck-like protein containing a CARD
83	NM_024602	hypothetical protein FLJ21156
84	NM_005080	X-box binding protein 1
85	NM_004050	BCL2-like 2
86	NM_014454	p53 regulated PA26 nuclear protein
87	W28438	chromosome 14 open reading frame 78
88	XM_008802	RBBP8
89	XM_053627	FGF4
90	NM_006727	cadherin 10, type 2 (T2-cadherin)
91	NM_005980	S100 calcium binding protein P

92	XM_050665	FH
93	NM_000432	myosin, light polypeptide 2, regulatory, cardiac, slow
94	D16815	nuclear receptor subfamily 1, group D, member 2
95	XM_044825	SUPT3H
96	NM_058179	phosphoserine aminotransferase
97	XM_018112	RBBP4
98	NM_020386	HRAS-like suppressor
99	AK057758	insulin receptor substrate 3-like
100	XM_044111	RIT1
101	NM_004313	arrestin, beta 2
102	L26584	Ras protein-specific guanine nucleotide-releasing factor 1
103	NM_005414	SKI-like
104	XM_031603	BUB1B
105	XM_015963	SDFR1
106	NM_002415	macrophage migration inhibitory factor (glycosylation-inhibiting factor)
107	NM_078487	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)
108	XM_047707	KIAA1265
109	NM_001065	tumor necrosis factor receptor superfamily, member 1A
110	XM_045104	LGALS3BP
111	AI053741	Homo sapiens, clone IMAGE:4826963, mRNA
112	NM_003600	serine/threonine kinase 6
113	NM_012112	chromosome 20 open reading frame 1
114	NM_000387	solute carrier family 25 (carnitine/acylcarnitine translocase), member 20
115	NM_005587	MADS box transcription enhancer factor 2, polypeptide A (myocyte enhancer factor
116	NM_001892	casein kinase 1, alpha 1
117	NM_016277	RAB23, member RAS oncogene family
118	NM_003094	small nuclear ribonucleoprotein polypeptide E
119	NM_006623	phosphoglycerate dehydrogenase
120	NM_005441	chromatin assembly factor 1, subunit B (p60)
121	NM_002659	plasminogen activator, urokinase receptor
122	NM_000057	Bloom syndrome
123	NM_001202	bone morphogenetic protein 4
124	NM_003289	tropomyosin 2 (beta)
125	XM_003325	CCNA2
126	XM_032813	HUMGT198A
127	NM_006403	enhancer of filamentation 1
128	NM_006289	talin 1
129	NM_003405	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta poly
130	NM_000368	tuberous sclerosis 1
131	BC008826	PAX3
132	NM_003908	eukaryotic translation initiation factor 2, subunit 2 beta, 38kDa
133	NM_004282	BCL2-associated athanogene 2
134	XM_010777	ICAP-1A
135	XM_034350	ANXA3
136	NM_004965	high-mobility group nucleosome binding domain 1
137	NM_001216	carbonic anhydrase IX
138	NM_006325	RAN, member RAS oncogene family
139	NM_006516	solute carrier family 2 (facilitated glucose transporter), member 1

140	NM_003657	breast carcinoma amplified sequence 1
141	NM_004417	dual specificity phosphatase 1
142	M94362	LMNB2
143	XM_057994	SDHA
144	XM_043451	PIM1
145	NM_021005	nuclear receptor subfamily 2, group F, member 2
146	XM_049928	CARD14
147	AA017553	ESTs
148	NM_004905	antioxidant protein 2
149	NM_001274	CHK1 checkpoint homolog (S. pombe)
150	NM_002483	carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross re
151	XM_045049	TNFSF10
152	XM_007770	FLJ20171
153	NM_015926	putative secreted protein ZSIG11
154	NM_005348	heat shock 90kDa protein 1, alpha
155	NM_003567	breast cancer anti-estrogen resistance 3
156	NM_002507	nerve growth factor receptor (TNFR superfamily, member 16)
157	XM_029216	APEX2
158	NM_005654	nuclear receptor subfamily 2, group F, member 1
159	XM_009873	MMP11
160	NM_002105	H2A histone family, member X
161	NM_001827	CDC28 protein kinase regulatory subunit 2
162	XM_050486	NOC4
163	XM_015513	SNRPG
164	AB037759	eukaryotic translation initiation factor 2 alpha kinase 4
165	NM_000122	excision repair cross-complementing rodent repair deficiency, complementation gr
166	NM_006218	phosphoinositide-3-kinase, catalytic, alpha polypeptide
167	NM_003127	spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)
168	NM_031265	mucin and cadherin-like
169	NM_016531	Kruppel-like factor 3 (basic)
170	NM_002629	phosphoglycerate mutase 1 (brain)
171	NM_003152	signal transducer and activator of transcription 5A
172	NM_002037	FYN oncogene related to SRC, FGR, YES
173	NM_002607	platelet-derived growth factor alpha polypeptide
174	XM_003560	MAD2L1
175	NM_052888	KIAA0563-related gene
176	NM_001348	death-associated protein kinase 3
177	NM_003883	histone deacetylase 3
178	NM_001659	ADP-ribosylation factor 3
179	NM_033379	CDC2
180	XM_031718	EHD4
181	NM_014977	apoptotic chromatin condensation inducer in the nucleus
182	NM_006570	Ras-related GTP-binding protein
183	NM_002466	v-myb myeloblastosis viral oncogene homolog (avian)-like 2
184	NM_001949	E2F transcription factor 3
185	XM_018149	SELT
186	NM_013277	Rac GTPase activating protein 1
187	NM_014060	MCT-1 protein
188	NM_003684	MAP kinase-interacting serine/threonine kinase 1
189	NM_031966	cyclin B1
190	XM_012601	MNT

191	NM_005657	tumor protein p53 binding protein, 1
192	XM_051583	RAF1
193	NM_001255	CDC20 cell division cycle 20 homolog (S. cerevisiae)
194	NM_030808	LIS1-interacting protein NUDEL; endooligopeptidase A
195	NM_032989	BCL2-antagonist of cell death
196	XM_011577	STK17A
197	NM_003925	methyl-CpG binding domain protein 4
198	NM_016587	chromobox homolog 3 (HP1 gamma homolog, Drosophila)
199	NM_006870	destrin (actin depolymerizing factor)
200	XM_008313	LOC146870
201	NM_006812	amplified in osteosarcoma
202	NM_003183	a disintegrin and metalloproteinase domain 17 (tumor necrosis factor, alpha, con
203	XM_052798	CDC25C
204	NM_002626	phosphofructokinase, liver
205	NM_033292	caspase 1, apoptosis-related cysteine protease (interleukin 1, beta, convertase)
206	XM_006961	CHD4
207	NM_000269	non-metastatic cells 1, protein (NM23A) expressed in
208	NM_004873	BCL2-associated athanogene 5
209	NM_001034	ribonucleotide reductase M2 polypeptide
210	NM_003070	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subf
211	NM_006595	apoptosis inhibitor 5
212	XM_040402	CPNE3
213	NM_007111	transcription factor Dp-1
214	NM_003597	TGFB inducible early growth response 2
215	NM_002741	protein kinase C-like 1
216	NM_021138	TNF receptor-associated factor 2
217	XM_054954	CCNF
218	NM_003879	CASP8 and FADD-like apoptosis regulator
219	NM_002089	chemokine (C-X-C motif) ligand 2
220	BC018118	Rho GTPase activating protein 1
221	XM_007070	TBC1D4
222	NM_032094	protocadherin gamma subfamily A, 12
223	NM_003472	DEK oncogene (DNA binding)
224	XM_036063	LOC204666
225	XM_006197	E2IG4
226	NM_002198	interferon regulatory factor 1
227	NM_003639	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma
228	XM_010826	LOC150584
229	NM_006393	nebulette
230	NM_020436	sal-like 4 (Drosophila)
231	XM_038427	FES
232	NM_032984	caspase 2, apoptosis-related cysteine protease (neural precursor cell expressed,
233	NM_002093	glycogen synthase kinase 3 beta
234	XM_043782	E2F4
235	XM_058230	JUND
236	XM_071388	PPFIA2
237	XM_056931	B3GNT1
238	NM_002357	MAX dimerization protein 1

239	NM_024320	hypothetical protein MGC11242
240	NM_006763	BTG family, member 2
241	NM_000244	multiple endocrine neoplasia I
242	XM_017741	FSCN1
243	W02608	ESTs, Weakly similar to hypothetical protein FLJ20378 [Homo sapiens] [H.sapiens
244	XM_044910	SNRPB
245	NM_033339	caspase 7, apoptosis-related cysteine protease
246	NM_001712	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)
247	NM_031993	protocadherin gamma subfamily A, 1
248	NM_002616	period homolog 1 (Drosophila)
249	XM_001357	MYCBP
250	NM_031295	Williams Beuren syndrome chromosome region 21
251	NM_001110	a disintegrin and metalloproteinase domain 10
252	NM_004359	cell division cycle 34
253	NM_003667	G protein-coupled receptor 49
254	XM_027651	TNFRSF10B
255	NM_012165	F-box and WD-40 domain protein 3
256	XM_009475	AHCY
257	XM_035145	LXN
258	NM_000365	TPI1
259	NM_003994	KIT ligand
260	NM_004341	carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotase
261	XM_039754	RAB10
262	AF346509	NFAT5
263	XM_071453	YWHAE
264	NM_006701	similar to S. pombe dim1+
265	NM_024854	hypothetical protein FLJ22028
266	NM_004964	histone deacetylase 1
267	NM_007194	CHK2 checkpoint homolog (S. pombe)
268	NM_007168	ATP-binding cassette, sub-family A (ABC1), member 8
269	XM_033064	ST5
270	NM_003841	tumor necrosis factor receptor superfamily, member 10c, decoy without an intrace
271	XM_031287	CXCL3
272	NM_003535	H3FJ
273	U82467	tubby homolog (mouse)
274	XM_017134	BRCA2
275	NM_014784	Rho guanine nucleotide exchange factor (GEF) 11
276	NM_005438	FOS-like antigen 1
277	NM_006107	acid-inducible phosphoprotein
278	NM_012323	v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)
279	XM_002116	SFN
280	NM_006286	transcription factor Dp-2 (E2F dimerization partner 2)
281	XM_046643	NXT1
282	AA406526	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 2344436.
283	NM_020637	fibroblast growth factor 22
284	NM_005375	v-myb myeloblastosis viral oncogene homolog (avian)
285	NM_012466	tetraspanin TM4-B

286	XM_002636	IGFBP2
287	AB037845	Rho-GTPase activating protein 10
288	NM_005983	S-phase kinase-associated protein 2 (p45)
289	AF308602	Notch homolog 1, translocation-associated (Drosophila)
290	NM_014318	apoptosis related protein
291	NM_000207	insulin
292	XM_043799	MPZL1
293	XM_010208	PIM2
294	XM_045613	EHD1
295	NM_018948	Gene 33/Mig-6
296	XM_015547	LATS1
297	NM_014248	ring-box 1
298	NM_003558	phosphatidylinositol-4-phosphate 5-kinase, type I, beta
299	XM_033878	TIMP1
300	NM_007315	signal transducer and activator of transcription 1, 91kDa
301	NM_000679	adrenergic, alpha-1B-, receptor
302	XM_036588	SDCCAG33
303	NM_004078	cysteine and glycine-rich protein 1
304	XM_050512	ACVR1
305	XM_028205	GLP1R
306	XM_071498	E2F6
307	AA100736	hypothetical protein DKFZp434D0215
308	NM_005253	FOS-like antigen 2
309	XM_041335	SCAP2
310	AF110908	TNF receptor-associated factor 3
311	XM_058227	ZK1
312	XM_049776	DSCAM
313	XM_045802	PXN
314	XM_058125	UBF-fl
315	NM_005385	natural killer-tumor recognition sequence
316	NM_002745	mitogen-activated protein kinase 1
317	XM_031413	TIAF1
318	NM_020249	a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin typ
319	XM_046179	ID1
320	XM_007245	YY1
321	AI972873	SH3 domain binding glutamic acid-rich protein like 2
322	XM_047494	UGDH
323	NM_022161	baculoviral IAP repeat-containing 7 (livin)
324	NM_004493	hydroxyacyl-Coenzyme A dehydrogenase, type II
325	XM_009915	LIF
326	BF343776	glutathione reductase
327	NM_004725	BUB3 budding uninhibited by benzimidazoles 3 homolog (yeast)
328	XM_008855	NR2F6
329	NM_018640	neuronal specific transcription factor DAT1
330	XM_013050	BIRC4
331	XM_003222	CTNNB1
332	NM_016316	REV1-like (yeast)
333	NM_012098	angiopoietin-like 2
334	XM_058285	CD24
335	NM_004040	ras homolog gene family, member B
336	XM_043785	NOL3

337	NM_032471	protein kinase (cAMP-dependent, catalytic) inhibitor beta
338	NM_022873	interferon, alpha-inducible protein (clone IFI-6-16)
339	XM_035114	KIAA1277
340	XM_007722	CHD2
341	NM_006054	reticulon 3
342	XM_054920	KIAA0828
343	NM_001895	casein kinase 2, alpha 1 polypeptide
344	NM_032365	PRO2000
345	XM_010040	ARHGAP8
346	NM_005419	signal transducer and activator of transcription 2, 113kDa
347	NM_003299	tumor rejection antigen (gp96) 1
348	XM_042423	EMP1
349	AF207547	LATS, large tumor suppressor, homolog 2 (Drosophila)
350	NM_002878	RAD51-like 3 (S. cerevisiae)
351	XM_010914	PCAF
352	XM_038418	PRC1
353	Z18817	heat shock 70kDa protein 4
354	U70451	myeloid differentiation primary response gene (88)
355	NM_002957	retinoid X receptor, alpha
356	XM_046041	CCT2
357	XM_028620	HOXC9
358	XM_012894	ZNF14
359	NM_021979	heat shock 70kDa protein 2
360	NM_005163	v-akt murine thymoma viral oncogene homolog 1
361	XM_006299	API5
362	NM_001388	developmentally regulated GTP binding protein 2
363	NM_004992	methyl CpG binding protein 2 (Rett syndrome)
364	XM_016845	HHGP
365	AK054731	tubulin, alpha 1 (testis specific)
366	XM_003628	CCNG2
367	NM_000291	phosphoglycerate kinase 1
368	XM_044653	EGFR
369	XM_046245	PIG8
370	NM_007229	protein kinase C and casein kinase substrate in neurons 2
371	NM_033637	beta-transducin repeat containing
372	XM_033862	ELK1
373	NM_000638	vitronectin (serum spreading factor, somatomedin B, complement S-protein)
374	NM_018098	epithelial cell transforming sequence 2 oncogene
375	NM_001880	activating transcription factor 2
376	NM_003122	serine protease inhibitor, Kazal type 1
377	XM_008055	COX4I1
378	XM_046881	SLC9A1
379	NM_003860	barrier to autointegration factor 1
380	XM_003029	ITGB5
381	NM_005566	lactate dehydrogenase A
382	NM_019113	fibroblast growth factor 21
383	XM_030478	SVIL
384	NM_006167	NK3 transcription factor related, locus 1 (Drosophila)
385	NM_007324	MAD, mothers against decapentaplegic homolog (Drosophila) interacting protein, r
386	NM_002342	lymphotoxin beta receptor (TNFR superfamily, member 3)

387	NM_002909	regenerating islet-derived 1 alpha (pancreatic stone protein, pancreatic thread
388	XM_041552	RAD17
389	NM_030662	mitogen-activated protein kinase kinase 2
390	NM_022333	TIA1 cytotoxic granule-associated RNA binding protein-like 1
391	XM_037682	SMARCB1
392	XM_033932	FLJ20485
393	BC002513	eukaryotic translation initiation factor 2, subunit 1 alpha, 35kDa
394	NM_003470	ubiquitin specific protease 7 (herpes virus-associated)
395	NM_001320	casein kinase 2, beta polypeptide
396	AA527919	Homo sapiens, clone IMAGE:5285034, mRNA
397	NM_005167	hypothetical protein MGC19531
398	XM_045642	SF1
399	XM_029816	YWHAB
400	NM_006121	keratin 1 (epidermolytic hyperkeratosis)
401	NM_004843	class I cytokine receptor
402	NM_000450	selectin E (endothelial adhesion molecule 1)
403	NM_013374	programmed cell death 6 interacting protein
404	AK024858	hypothetical protein LOC221496
405	XM_006890	ELK3
406	NM_022870	myosin, heavy polypeptide 11, smooth muscle
407	XM_033910	TCP1
408	XM_030523	MAP3K8
409	NM_003821	receptor-interacting serine-threonine kinase 2
410	XM_002633	MYCN
411	NM_002087	granulin
412	NM_007019	ubiquitin-conjugating enzyme E2C
413	AI685200	DKFZP586G1517 protein
414	XM_009203	AKT2
415	NM_013986	Ewing sarcoma breakpoint region 1
416	NM_004208	programmed cell death 8 (apoptosis-inducing factor)
417	XM_011791	LAMC3
418	NM_022746	hypothetical protein FLJ22390
419	AL042759	NADPH oxidase organizer 1
420	NM_003808	tumor necrosis factor (ligand) superfamily, member 13
421	XM_002562	VAMP5
422	NM_005923	mitogen-activated protein kinase kinase kinase 5
423	NM_001315	mitogen-activated protein kinase 14
424	NM_007022	putative tumor suppressor 101F6
425	XM_047007	PLAGL2
426	NM_005556	keratin 7
427	NM_000454	superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult))
428	AI886326	hypothetical protein FLJ21195 similar to protein related to DAC and cerberus
429	NM_005917	malate dehydrogenase 1, NAD (soluble)
430	NM_002835	protein tyrosine phosphatase, non-receptor type 12
431	NM_005972	pancreatic polypeptide receptor 1
432	NM_016328	GTF2I repeat domain containing 1
433	NM_000860	hydroxyprostaglandin dehydrogenase 15-(NAD)
434	NM_003882	WNT1 inducible signaling pathway protein 1
435	XM_028817	ADCY6
436	NM_000955	prostaglandin E receptor 1 (subtype EP1), 42kDa

437	X68560	Sp3 transcription factor
438	NM_006443	putative c-Myc-responsive
439	NM_001090	ATP-binding cassette, sub-family F (GCN20), member 1
440	NM_002827	protein tyrosine phosphatase, non-receptor type 1
441	XM_034007	BCAR1
442	NM_005901	MAD, mothers against decapentaplegic homolog 2 (Drosophila)
443	NM_001963	epidermal growth factor (beta-urogastrone)
444	BM044930	neuronal guanine nucleotide exchange factor
445	NM_004701	cyclin B2
446	XM_002375	IL1F8
447	NM_001945	diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth f
448	NM_000230	leptin (obesity homolog, mouse)
449	NM_001903	catenin (cadherin-associated protein), alpha 1, 102kDa
450	NM_002220	inositol 1,4,5-trisphosphate 3-kinase A
451	NM_020384	claudin 2
452	NM_002734	protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extin
453	NM_020243	translocase of outer mitochondrial membrane 22 homolog (yeast)
454	NM_004380	CREB binding protein (Rubinstein-Taybi syndrome)
455	XM_044659	CSK
456	NM_002875	RAD51 homolog (RecA homolog, E. coli) (S. cerevisiae)
457	XM_033428	AK1
458	NM_005745	accessory protein BAP31
459	NM_030753	wingless-type MMTV integration site family, member 3
460	XM_034587	FLJ22174
461	NM_004920	AATK
462	NM_007065	CDC37 cell division cycle 37 homolog (S. cerevisiae)
463	NM_001239	cyclin H
464	XM_036323	TSG101
465	NM_001233	caveolin 2
466	XM_015956	CTBP2
467	XM_015505	AXL
468	NM_003749	insulin receptor substrate 2
469	XM_016033	DPF3
470	NM_004889	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit f, isoform 2
471	XM_003213	NS
472	XM_033761	COBL
473	XM_047049	E2F1
474	NM_006572	guanine nucleotide binding protein (G protein), alpha 13
475	NM_006024	Tax1 (human T-cell leukemia virus type I) binding protein 1
476	NM_016245	retinal short-chain dehydrogenase/reductase 2
477	XM_010339	GPC4
478	NM_002129	high-mobility group box 2
479	NM_006565	CCCTC-binding factor (zinc finger protein)
480	AL137667	MAPK8
481	XM_050236	LENG4
482	NM_005805	26S proteasome-associated pad1 homolog
483	XM_054928	CLN8
484	NM_001350	death-associated protein 6

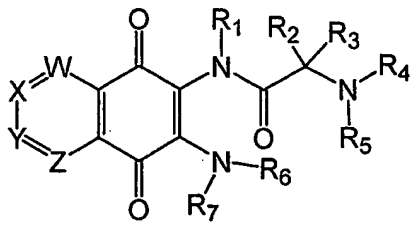
485	NM_016073	likely ortholog of mouse hepatoma-derived growth factor, related protein 3
486	XM_031926	NFKB2
487	NM_005085	nucleoporin 214kDa
488	NM_003904	zinc finger protein 259
489	NM_014397	NIMA (never in mitosis gene a)-related kinase 6
490	XM_017096	ABR
491	XM_003477	FAT
492	NM_001982	v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian)
493	NM_006705	growth arrest and DNA-damage-inducible, gamma
494	NM_004958	FK506 binding protein 12-rapamycin associated protein 1
495	XM_004713	FLNC
496	NM_021235	epidermal growth factor receptor substrate EPS15R
497	XM_030044	CSE1L
498	AI685466	LOC90353
499	NM_003311	tumor suppressing subtransferable candidate 3
500	XM_039984	CNOT8
501	XM_001831	CYR61
502	XM_052827	CFL2
503	XM_007487	ASB2
504	XM_003405	HD
505	XM_012723	C18orf1
506	NM_005564	lipocalin 2 (oncogene 24p3)
507	XM_010767	NCKAP1
508	NM_001324	cleavage stimulation factor, 3' pre-RNA, subunit 1, 50kDa
509	NM_005658	TNF receptor-associated factor 1
510	NM_000168	GLI-Kruppel family member GLI3 (Greig cephalopolysyndactyly syndrome)
511	XM_027639	DKFZP434J214
512	XM_033445	SLC7A7
513	NM_000852	glutathione S-transferase pi
514	NM_002097	general transcription factor IIIA
515	NM_003243	transforming growth factor, beta receptor III (betaglycan, 300kDa)
516	XM_003444	FGF5
517	XM_035107	BRAF
518	D55886	adenylate cyclase 5
519	NM_005633	son of sevenless homolog 1 (Drosophila)
520	AI161049	voltage-dependent calcium channel gamma subunit-like protein
521	XM_045460	CDC25B
522	AA634799	Homo sapiens cDNA: FLJ22864 fis, clone KAT02164.
523	NM_004230	endothelial differentiation, sphingolipid G-protein-coupled receptor, 5
524	XM_040912	AMN
525	XM_056595	OTOF
526	XM_054160	VMD2
527	XM_049935	CTEN
528	NM_006365	transcriptional activator of the c-fos promoter
529	XM_027186	WNT2
530	NM_001067	topoisomerase (DNA) II alpha 170kDa
531	XM_044785	KCNJ13
532	XM_007585	TJP1

533	XM_042940	UNC5C
534	XM_037408	BAP1
535	XM_005428	1-Dec
536	NM_014452	tumor necrosis factor receptor superfamily, member 21
537	NM_006645	serologically defined colon cancer antigen 28
538	XM_031972	CNNM2
539	XM_047561	ARHA
540	XM_046191	CGI-31
541	NM_003778	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 4
542	XM_011713	COPS5
543	NM_032957	tumor necrosis factor receptor superfamily, member 6b, decoy
544	NM_006044	histone deacetylase 6
545	NM_021144	PC4 and SFRS1 interacting protein 1
546	AA531287	ESTs
547	XM_033355	ABL1
548	XM_008394	EZH1
549	XM_036570	TNFRSF12A
550	XM_031209	IL1F9
551	XM_027311	BFAR
552	NM_006166	nuclear transcription factor Y, beta
553	XM_043103	HSD11B2
554	XM_050735	ST14
555	NM_057159	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2
556	NM_001702	brain-specific angiogenesis inhibitor 1
557	NM_005312	guanine nucleotide-releasing factor 2 (specific for crk proto-oncogene)
558	NM_001042	solute carrier family 2 (facilitated glucose transporter), member 4
559	L41944	interferon (alpha, beta and omega) receptor 2
560	NM_000264	patched homolog (Drosophila)
561	XM_041744	IER3
562	NM_005967	NGFI-A binding protein 2 (EGR1 binding protein 2)
563	XM_009170	CEACAM7
564	NM_004231	ATPase, H+ transporting, lysosomal 14kDa, V1 subunit F
565	NM_004315	N-acylsphingosine amidohydrolase (acid ceramidase) 1
566	XM_008654	MAP2K4
567	XM_041847	TNF
568	XM_040448	RAD1
569	XM_011068	MST1R
570	NM_000662	N-acetyltransferase 1 (arylamine N-acetyltransferase)
571	XM_001744	TNFRSF8
572	XM_028038	BMPR2
573	NM_006534	nuclear receptor coactivator 3
574	NM_005091	peptidoglycan recognition protein
575	NM_024426	Wilms tumor 1
576	AA290601	hypothetical protein LOC137075
577	AI810669	ESTs, Moderately similar to hypothetical protein FLJ20378 [Homo sapiens] [H.sap
578	NM_003550	MAD1 mitotic arrest deficient-like 1 (yeast)
579	NM_012415	RAD54B homolog
580	XM_033469	TGFBR2

581	XM_039779	CAPRI
582	XM_049512	TRIP13
583	NM_002969	mitogen-activated protein kinase 12
584	NM_005380	neuroblastoma, suppression of tumorigenicity 1
585	XM_029490	DPH2L1
586	AL136835	Toll-interacting protein
587	XM_034567	CCND2
588	NM_032192	protein phosphatase 1, regulatory (inhibitor) subunit 1B (dopamine and cAMP regu
589	NM_000072	CD36 antigen (collagen type I receptor, thrombospondin receptor)

WHAT IS CLAIMED IS:

1. A compound having the structure of Formula (I)



Formula I

wherein

W, X, Y and Z are each selected from a bond, CH, C-R_8, C-R_9, C-R_{10}, C-R_{11}, O (oxygen), N (nitrogen) and S (sulfur) and no more than two of W, X, Y and Z are simultaneously O, N and S;

wherein, R_8, R_9, R_{10}, R_{11} are each selected from hydrogen, hydroxyl, sulfhydryl, alkoxy, thioalkoxy, alkyl, halogen, CN, CF_3, NO_2, $COOR_{12}$, $CONR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{12}COR_{13}$, $NR_{12}SO_2R_{13}$ and $NR_{14}CONR_{12}R_{13}$;

wherein R_{12}, R_{13} and R_{14} are each selected from hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl and heterocycloalkyl;

and wherein $NR_{12}R_{13}$ is further optionally selected from substituted and unsubstituted mono or bicyclic ring with one to four heteroatoms such as N, O and S;

and further wherein R_{12} and R_{14} may form a 4, 5, 6 or 7-membered cyclic ring system;

wherein R_1, R_2, R_3, R_4, and R_5 are each selected from hydrogen, alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted polyaromatic ring, substituted or unsubstituted heteroaromatic ring having hetero atom(s) selected from N, O and S, substituted or unsubstituted aralkyl, substituted or unsubstituted, cyclic or polycyclic, hydrocarbon and substituted or unsubstituted, monoheterocycle or polyheterocycle (of 3-8 atoms per ring) having one to four hetero atoms selected from N, O, and S; and

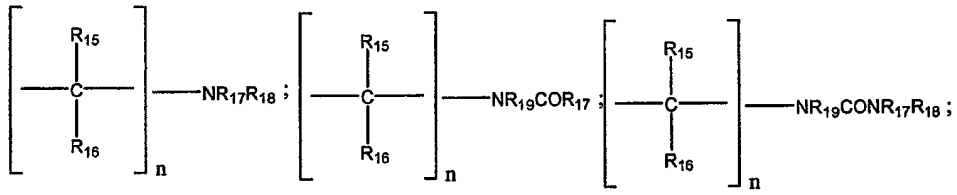
and wherein said substitutions are selected from hydrogen, hydroxyl, sulfhydryl, alkoxy, thioalkoxy, alkyl, halogen, CN, CF_3, NO_2, $COOR_{12}$, $CONR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{12}COR_{13}$, $NR_{12}SO_2R_{13}$, and $NR_{14}CONR_{12}R_{13}$;

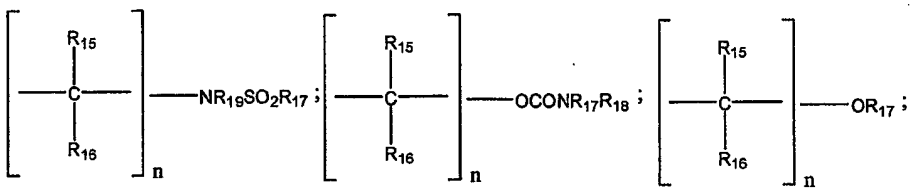
wherein R_{12}, R_{13} and R_{14} are each selected from hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, and heterocycloalkyl;

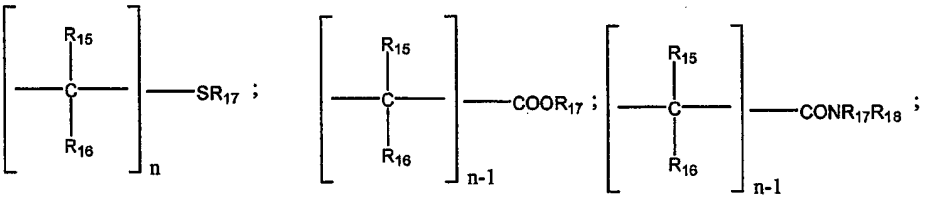
and wherein $NR_{12}R_{13}$ may form a substituted and unsubstituted, mono or bicyclic ring with one to four heteroatoms selected from N, O and S;

and wherein R_{12} and R_{14} may form a 4, 5, 6 or 7-member cyclic ring system;

and wherein R_1, R_4, R_5, R_6 and R_7 are also selected from:







where n is 2, 3 or 4 and R_{15}, R_{16}, R_{17}, R_{18} and R_{19} are each selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted aryl, unsubstituted or substituted heteroaryl, and unsubstituted or substituted alkylaryl;

$NR_{17}R_{18}$ may form a substituted or unsubstituted, mono or bicyclic ring with one to four heteroatoms selected from N, O and S;

and wherein R_{17} and R_{19} may form a 4, 5, 6 or 7-membered cyclic ring system;

and wherein R_4 may also be selected from $-COR_{17}$, $-SO_2R_{17}$, $-CONR_{17}R_{18}$ and $-C(=NR_{19})NR_{17}R_{18}$;

and wherein R_6 and R_7 are each selected from:

alkyl, substituted and unsubstituted phenyl or polyaromatic, substituted or unsubstituted heteroaromatic, wherein said hetero atom is selected from N, O and S, substituted or unsubstituted aralkyl, and substituted or unsubstituted, cyclic or polycyclic hydrocarbon, or mono- or poly-heterocycle of 3 to 8 atom rings having one to four hetero atoms selected from N, O and S; and

wherein said substitutions are selected from hydroxyl, sulfhydryl, alkoxy, thioalkoxy, alkyl, halogen, CN, CF_3, NO_2, $COOR_{12}$, $CONR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{12}COR_{13}$, $NR_{12}SO_2R_{13}$ and $NR_{14}CONR_{12}R_{13}$;

wherein R_{12}, R_{13} and R_{14} are each selected from hydrogen, alkyl, heteroalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, and heterocycloalkyl;

and wherein $NR_{12}R_{13}$ may form a substituted or unsubstituted, mono or bicyclic, ring with one to four heteroatoms selected from N, O and S;

and wherein NR_4R_5 and NR_6R_7 may each be selected from substituted and unsubstituted, mono or bicyclic, rings comprising one to four heteroatoms selected from N, O and S and wherein said N may also be substituted or unsubstituted,

and including salts thereof.

2. The compound of claim 1 wherein W and Z are each C-R_8, C-R_{11} or N and wherein X and Y are each C-R_9 or C-R_{10}.

3. The compound of claim 1 wherein X and Y are each C-R_9, C-R_{10} or N and wherein W and Z are each C-R_8 or C-R_{11}.

4. The compound of claim 1 wherein W is C-R_8 or N and wherein X, Y and Z are each C-R_9, C-R_{10} or C-R_{11}.

5. The compound of claim 1 wherein Z is C-R_{11} or N and wherein W, Y and Z are each C-R_8, C-R_9 or C-R_{10}.

6. The compound of claim 1 wherein X is C-R_9 or N and wherein W, Y and Z are each C-R_8, C-R_{10} or C-R_{11}.

7. The compound of claim 1 wherein Y is C-R_{10} or N and wherein W, X, and Z are each CH, C-R_8, C-R_9 or C-R_{11}.

8. The compound of claim 1 wherein W, X, Y and Z are each selected from CH, C-R_8, C-R_9, C-R_{10} and C-R_{11}.

9. The compound of claim 8 wherein W, X, Y and Z are each CH.

10. The compound of claim 1 wherein R_2 and R_3 are each selected from hydrogen, lower alkyl of 1-6 carbons and aryl.

11. The compound of claim 1 wherein R_1 is selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and –alkylpyrrolidine, and wherein R_2 and R_3 are each hydrogen, lower alkyl (1-6 carbon) or aryl.

12. The compound of claim 1 wherein R_4 and R_5 are each selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, --alkylmorpholine, -alkylpiperizine, -alkypiperidine, and –alkylpyrrolidine, or wherein $-NR_4R_5$ is a substituted or unsubstituted, monocyclic or bicyclic, heterocycloalkyl ring, and wherein R_2 and R_3 are each selected from hydrogen, lower alkyl (1-6 carbon) and aryl.

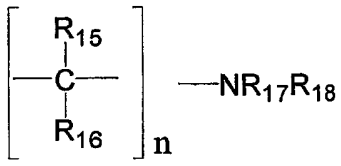
13. The compound of claim 1 wherein R_6 and R_7 are selected from alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and –alkylpyrrolidine, and R_2 and R_3 are selected from hydrogen, lower alkyl (1-6 carbon) and aryl.

14. The compound of claim 9 wherein R_2 and R_3 are selected from hydrogen, lower alkyl (1-6 carbon) and aryl.

15. The compound of claim 9 wherein R_1, R_4 and R_5 are each selected from hydrogen, alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted benzyl, methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl-, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, -methylpyrrole, -ethylpyrrole, -methylfuran, -ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and –alkylpyrrolidine, or wherein $-NR_4R_5$ is a substituted or unsubstituted, monocyclic or bicyclic, heterocycloalkyl ring, and wherein R_2 and R_3 are each hydrogen, lower alkyl (1-6 carbon) or aryl and wherein R_6 and R_7 are each selected from alkyl, cycloalkyl, unsubstituted or substituted phenyl, unsubstituted or substituted

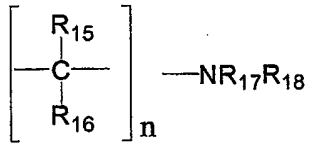
benzyl, -methylpyridine, -ethylpyridine, -methylindole, -ethylindole, alkoxyethyl-, hydroxyethyl, N,N-dialkyl-ethyl, N,N-dialkyl-propyl, -methylpyrrole, -ethylpyrrole, -methylfuran,- ethylfuran, -alkylmorpholine, -alkylpiperizine, -alkypiperidine, and -alkylpyrrolidine.

16. The compound of claim 1 wherein R_2 and R_3 are each selected from hydrogen and alkyl, and wherein R_4 and R_6 are each selected from alkyl and



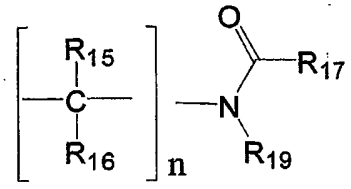
where n is 2 ,3 or 4 and one or both of R_5 and R_7 is alkyl.

17. The compound of claim 9 wherein R_1 is alkyl, wherein R_2 and R_3 are each selected from hydrogen and alkyl and wherein R_4 and R_6 are each selected from alkyl and



wherein n is 2, 3 or 4 and one or both of R_5 and R_7 is alkyl.

18. The compound of claim 1 wherein R_2 and R_3 are each selected from hydrogen and alkyl, wherein R_4 and R_6 are each selected from alkyl and

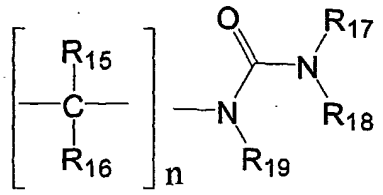


wherein n is 2, 3 or 4 and one or both of R_5 and R_7 is alkyl.

19. The compound of claim 1 wherein

R_2 and R_3 are each selected from hydrogen and alkyl

wherein R_4 and R_6 are each selected from alkyl and

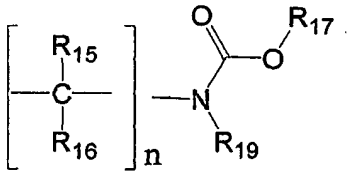


where n is 2, 3 or 4 and one or both of R_5 and R_7 is alkyl

20. Compound of claim 1wherein

R_2 and R_3 are each selected from hydrogen and alkyl

R_4 and R_6 are each selected from alkyl and

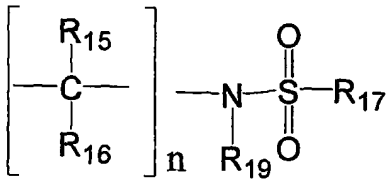


where n is 2,3 or 4 and one or both of R_5 and R_7 is alkyl.

21. The compound of claim 1 wherein

R_2 and R_3 are each selected from hydrogen and alkyl

R_4 and R_6 are each selected from alkyl and

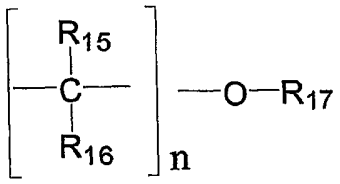


where n is 2, 3 or 4 and one or both of R_5 and R_7 is alkyl.

22. The compound of claim 1 wherein

R_2 and R_3 are each selected from hydrogen and alkyl,

R_4 and R_6 are each selected from alkyl and



where n is 2, 3 or 4 and one or both of R_5 and R_7 is alkyl.

23. The compound of claim 1 wherein R_1 is methyl.

24. The compound of claim 9 wherein R_1 is methyl.

25. The compound of claim 1 wherein R_1, R_6 and R_7 are methyl.

26. The compound of claim 9 wherein R_1, R_6, and R_7 are methyl.

27. The compound of claim 23 wherein $-NR_4R_5$ is a substituted or unsubstituted, monocyclic or bicyclic, heterocycloalkyl ring.

28. The compound of claim 25 wherein $-NR_4R_5$ is a substituted or unsubstituted, monocyclic or bicyclic, heterocycloalkyl ring.

29. The compound of claim 26 wherein $-NR_4R_5$ is a substituted or unsubstituted, monocyclic or bicyclic, heterocycloalkyl ring.

30. The compound of claim 26 wherein $-NR_4R_5$ is selected from aziridine, pyrrolidine, piperidine, hydroxy piperidine, morpholine, and N-methyl piperazine.

31. The compound of claim 23 wherein R_4 and R_5 are each lower alkylene-OR_{20} wherein R_{20} is hydrogen or lower alkyl.

32. The compound of claim 25 wherein R_4 and R_5 are each lower alkylene-OR20 wherein R_{20} is hydrogen or lower alkyl.

33. The compound of claim 26 wherein R_4 and R_5 are each lower alkylene-OR_{20} wherein R_{20} is hydrogen or lower alkyl.

34. A compound of claim 1 having a structure of Table 1 including salts thereof.

35. A compound of claim 1 having a structure of Table 2 including salts thereof.

36. A compound of claim 1 having a structure of Table 3 including salts thereof.

37. A compound of claim 1 having a structure of Table 4 including salts thereof.

38. A compound of claim 1 having a structure of Table 5 including salts thereof.

39. A compound of claim 1 having a structure of Table 6 including salts thereof.

40. A compound having a structure of Table 7 or Table 8 including salts thereof.

41. A compound having a structure of Table 9 or Table 10 including salts thereof.

42. A compound having a structure of Table 11 or Table 12 including salts thereof.

43. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier.

44. A method for preventing or treating a disease associated with a change in levels of expression of a set of genes in a mammal comprising administering to said mammal an effective amount of a compound of Claim 1.

45. A method for preventing or treating a disorder modulated by altered gene expression, wherein the disorder is selected from the group consisting of cancer, cardiovascular disorders, arthritis, osteoporosis, inflammation, periodontal disease and skin disorders, by administering to a mammal in need of such treatment a safe and effective amount of a compound according to Claim 1.

46. The method of Claim 45, wherein the disorder is cancer.

47. The method of claim 46 wherein said treatment prevents, arrests or reverts tumor growth and metastasis.

48. The method of claim 46 wherein said cancer is selected from the group consisting of solid tumors, lymphomas, skin cancer, urinary bladder cancer, breast cancer, uterine cancer, ovarian cancer, prostate cancer, lung cancer, colon cancer, rectum cancer, pancreatic cancer, kidney cancer, and stomach cancer.

49. The method of Claim 48 wherein the cancer is breast or colon cancer.

50. The method of claim 49 wherein said breast or colon cancer is adenocarcinoma.

51. The method of Claim 45 wherein the disorder is a cardiovascular disorder selected from the group consisting of dilated cardiomyopathy, congestive heart failure, atherosclerosis, plaque rupture, reperfusion injury, ischemia, chronic obstructive pulmonary disease, angioplasty restenosis, and aortic aneurysm.

52. A gene set wherein expression of each member of said gene set is modulated as a result of treatment with a compound of claim 1.

53. The gene set of claim 52 wherein expression of each member of said gene set is increased or each member of said gene set is decreased as a result of said treatment.

54. The gene set of claim 52 wherein the members of said gene set are selected from the genes identified in Table 19.

55. The gene set of claim 52 wherein said gene set is present in a cell.

56. A method for identifying an agent that modulates the expression of a gene set of claim 51, comprising:

(a) contacting a compound with a test system containing one or more polynucleotides corresponding to each of the members of the gene set of claim 52 under conditions wherein the members of said gene set are being expressed;

(b) determining a change in expression of each of said one or more polynucleotides of step (a) as a result of said contacting;

wherein said change in expression in step (b) indicates modulation of the members of said gene set thereby identifying said test compound as an agent that modulates the expression of said gene set.

57. The method of claim 56 wherein said change in expression is a decrease in expression of said one or more polynucleotides.

58. The method of claim 56 wherein said change in expression is a change in transcription of said one or more polynucleotides.

59. The method of claim 56 wherein said change in expression is determined by determining a change in activity of a polypeptide encoded by said polynucleotide.

60. The method of claim 56 wherein said one or more polynucleotides are present in a cell.

61. The method of claim 60 wherein said cell is a cancer cell.

62. The method of claim 60 wherein said cancer cell is a breast or colon cancer cell.

63. The method of claim 62 wherein said breast or colon cancer cell is an adenocarcinoma cancer cell.

64. The method of claim 60 wherein said cell is a recombinant cell engineered to contain said set of genes.

65. A set of genes comprising a plurality of subsets of genes wherein each subset of said plurality is a gene set identified by the method of claim 56.

66. Compounds identified as having activity using the method of claim 56.

67. The gene set of claim 51 wherein said gene set comprises a subset of the genes of Table 19.

68. The method of claim 56 wherein said compound modulates the expression of a subset of genes of Table 19.

69. A compound of claim 1 and having a structure of Table 13 and Table 14 including salts thereof.

70. A compound of claim 1 and having a structure of Table 15 and Table 16 including salts thereof.

71. A compound of claim 1 and having a structure of Table 17 and Table 18 including salts thereof.